



AGRICULTURAL RESEARCH INSTITUTE

PUSA

ACC No. 310792





# THE PHILIPPINE JOURNAL OF SCIENCE

ALVIN J. COX, M. A., PH. D.

GENERAL EDITOR

## SECTION B TROPICAL MEDICINE

EDITED WITH THE COOPERATION OF

J. A. JOHNSTON, M. D., DR. P. H.; OTTO SCHÖBL, M. D.  
STANTON YOUNGBERG, D. V. M.; H. W. WADE, M. D.

*Committee on Experimental Medicine*

J. D. LONG, A. M., M. D.; B. C. CROWELL, M. D.  
FERNANDO CALDERON, B. A., L. M.

*Committee on Clinical Medicine*

R. C. MCGREGOR, A. B.; H. E. KUPFER, A. B.

VOLUME XII

1917

WITH 10 PLATES AND 9 TEXT FIGURES



MANILA  
BUREAU OF PRINTING  
1917



## CONTENTS

### No. 1, January, 1917

	Page.
<b>SHAKLEE, ALFRED OGLE.</b> Experimental acclimatization to the tropical sun .....	1
<b>SCHÖBL, OTTO.</b> The influence of bile upon the distribution of cholera vibrios in the digestive system of experimental cholera carriers.....	28
<b>GARCIA, FAUSTINO.</b> Common intestinal parasites.....	25
<b>GUAZON, POTENCIANO.</b> A case of advanced pregnancy in the broad ligament .....	33
<b>Proceedings of the Manila Medical Society.....</b>	41

### No. 2, March, 1917

<b>SCHÖBL, OTTO, and PANGANIBAN, C. S.</b> Experimental cholera carriers and immunity .....	43
<b>MENDOZA-GUASON, MARIA PAZ.</b> Study of the anatomicopathologic lesions in one thousand Filipino children under five years.....	51
<b>CROWELL, B. C., and JOHNSTON, JOHN A.</b> Bacteriologic investigation of faeces and bile of cholera cases and cholera carriers.....	85
<b>Proceedings of the Manila Medical Society.....</b>	105

### No. 3, May, 1917

<b>JOHNSTON, JOHN A.</b> The varying morphology of <i>Bacillus lepræ</i> and the routine microscopic examination of nasal mucus in lepers.....	115
One plate.	
<b>ABRIOL, RUFINO.</b> Amoebic abscess of the liver among Filipinos.....	121
<b>MANLOVE, C. H.</b> Two cases of balantidial colitis.....	149
<b>Proceedings of the Manila Medical Society.....</b>	165

### No. 4, July, 1917

<b>MANALANG, C.</b> Degeneration of peripheral nerves.....	169
Two plates.	
<b>RUTH, EDWARD S., and GIBSON, ROBERT B.</b> Disappearance of the pigment in the melanophore of Philippine house lizards.....	181
Two plates.	
<b>LOWELL, PAUL MCC.</b> Essential factor in the treatment of pregnant cholera patients .....	191
<b>HILARIO, J. S., and WHARTON, L. D.</b> <i>Echinostoma ilocanum</i> (Garrison). A report of five cases and a contribution to the anatomy of the fluke..	203
One plate and 1 text figure.	

*Contents*

Page.

## No. 5, September, 1917

SCHÖBL, OTTO. A survey of certain chemicals with regard to their bactericidal action on cholera vibrios within the body of experimental cholera carriers .....	215
MANLOVE, C. H. Incidence of age, atheroma, and aneurisms as seen in autopsies of Filipinos.....	233
SCHÖBL, OTTO, and MONSERRAT, CARLOS. Substitution of human blood cells by monkey's red corpuscles in performing the complement fixation test for syphilis.....	249
Proceedings of the Manila Medical Society.....	255

## No. 6, November, 1917

GOMEZ, LIBORIO. Mohammedan medical practice in Cotabato Province....	261
One plate and 7 text figures.	
BOYNTON, WILLIAM HUTCHINS. A disease in cattle in the Philippine Islands similar to that caused by <i>Anaplasma marginale</i> Theiler.....	281
Three plates and 1 text figure.	
Proceedings of the Manila Medical Society.....	293
INDEX .....	297

THE PHILIPPINE  
JOURNAL OF SCIENCE  
B. TROPICAL MEDICINE

VOL. XII

JANUARY, 1917

No. 1

EXPERIMENTAL ACCLIMATIZATION TO THE TROPICAL SUN<sup>1</sup>

By ALFRED OGLE SHAKLEE

(From the Laboratory of Pharmacology, College of Medicine and Surgery,  
University of the Philippines, Manila)

INTRODUCTION

After a series of exposures of monkeys to the sun, Aron<sup>2</sup> concluded that the monkey was more susceptible to the action of the sun than any other animal with which he was acquainted, "including even the white man," and that monkeys exposed to the sun in a garden or on a roof in Manila die within seventy or eighty minutes, even though exposed in the early forenoon, in the coolest months of the year.

If this be true, the monkey ought to be an especially favorable subject for a study of acclimatization. I began such a study in October, 1911.

During the course of the experiments four objects were kept in view: (1) To see if the monkey gradually exposed to the sun would undergo a change which would enable it to live in the sun throughout a hot day; (2) if this change should take place, to learn its nature; (3) to determine the relative importance of the various meteorological factors which may combine to influence acclimatization; (4) to learn in how far extraneous factors, such as work, excitement, clothing, drugs, diet, and disease, may influence the course of events.

The monkeys used in this study were of the kind commonly obtainable in Manila. They are of two sizes and may be of two species. Probably both belong to the genus *Pithecius*.<sup>3</sup>

<sup>1</sup> Received for publication September 29, 1916. Read before the Philippine Islands Medical Association, November, 1912.

<sup>2</sup> This Journal, Sec. B (1911), 6, 110, 130.

<sup>3</sup> For the scientific names of Philippine monkeys, see Hellister, This Journal, Sec. D (1912), 7, 37; and Proc. U. S. Nat. Mus. (1914), 46, 328.

Experiments have been made almost daily for more than six months, including the hottest month known in Manila in six years (April, 1912). Twenty-three monkeys have been employed thus far.

The method of study was as follows: After a preliminary study of the variation of the monkey's body temperature in the shade, the monkey was placed in the sun rather early in the morning, and during the exposure, frequent observations were made of the pulse, respiration, and body temperature. Other symptoms were also looked for, such as position assumed, moisture of the skin, and signs of discomfort. Observations were also made upon the temperature of the atmosphere surrounding the monkey and the temperature of the surface upon which or near which it rested. The humidity of the atmosphere, reading of the black-bulb thermometer, and the amount of sunshine, as well as the velocity of the wind, were also noted. Monkeys were placed on the ground, on the asphalt roof of the laboratory, or upon slender poles raised above these surfaces. During the experiments the monkeys were kept upon a constant diet that seemed to be suitable, and they were offered water at frequent intervals. They were weighed daily. They were handled with great gentleness, and even the wildest soon ceased to show signs of fear. Overnight they were kept in clean cages.

## EXPERIMENTAL

### MONKEY 4

Monkey 4 seemed to show in the sun the typical reaction of a young, healthy Philippine monkey. Immediately below is a brief account of the main happenings in its experience during five months in the Manila sun.

This was a strong, active, healthy, wild male, which we surmised to be rather young. It weighed 1,528 grams when obtained, but within a few days it lost 100 grams. It has maintained practically constant weight ever since. We have not been able to detect in this monkey any signs of sickness. It has never suffered any significant injury. During the course of the experiments it has become much tamer.

A simple, wholesome diet, consisting of boiled white rice and raw ripe banana, was chosen. Twenty-five grams of each food for each kilogram of body weight were furnished the monkey at about the same hour once each day. Slight temporary changes in the diet from time to time did not seem to change the results.

At frequent intervals the monkey was given all the water it would drink.

The body temperature was taken at intervals through the day with a clinical thermometer, pushed well into the rectum and kept in place until there was no further rise. The monkey was excited as little as possible.

*Temperature of the monkey in the shade.*—The observations on this monkey's temperature were begun on the afternoon of November 27. The monkey was at first kept in the shade in the animal house (iron roof 3 to 5 meters high, no ceiling, well ventilated through netting). On November 28 the temperature both of the monkey and of the surrounding air was observed. The results of the observations are given in Table I.

TABLE I.—*Temperature of monkey 4 in shade in the animal house, November 28, 1911.*

Time.	Air tem- perature in house.	Body tempera- ture.
a. m.		
8.20	26	38.0
10.00	30	38.0
11.00	31	38.6
p. m.		
1.42	31.7	38.9
2.40	32	39.0
3.40	30	39.3
4.20	30.5	39.2

From Table I it is seen: (1) That there may be a rather marked rise in the body temperature of monkeys kept in the shade; that the body temperature began to rise between 10 and 11 o'clock, after the air temperature had reached 30° C., that is, after the air temperature had already risen 5°; (2) that, although the monkey remained in the sun throughout the day, about one half of the rise in body temperature occurred between 10 and 11 o'clock; (3) that it continued to rise gradually until 3.40 in the afternoon; (4) that between 2.40 and 3.40 in the afternoon the rise in body temperature was accompanied by a fall in air temperature; (5) that the maximum body temperature (39.3°) was apparently one hour later than the maximum air temperature (32°); (6) that the body temperature fell more slowly than the air temperature; (7) that this monkey's maximal normal body temperature is probably not below 39.5°, an observation in accord with the findings of Simpson and

Galbraith<sup>4</sup> for two other species of monkeys; (8) that there is apparently a wide variation in this monkey's normal temperature. This variation in body temperature seems to indicate, as has been observed in other monkeys, that the temperature-regulating mechanism of the monkey is not as efficient as is that of man. This suggests the possibility that, if the monkey can become adapted to life in the "tropical sun," man could more readily become adapted. The responsiveness of the monkey's temperature to external influences also suggests that the change in body temperature of an unacclimatized monkey might be a good index of the action of the sun upon the monkey and, possibly, an index of the sun's harmfulness for other animals, including man.

*The monkey is not injured by being seven hours in the sun.*—The first experimental exposure of this monkey to the sun was made on November 29, 1911. It was exposed to the sun at 8.35 in the forenoon on a horizontal pole resting 1 meter above a "skin" tennis court. It was free to walk back and forth. It received food at the usual hour, and water was given after taking the temperature.

The amount of sunshine recorded on this day at the Weather Bureau building, 0.3 kilometer distant, was nine hours and six minutes. If we take the Weather Bureau records, which would be approximately accurate for the tennis court, as a basis for our estimate, this monkey was exposed to the sun for five hours and twelve minutes before any clouds appeared, that is, from 8.35 in the forenoon to 1.47 in the afternoon. The clouds lasted eight minutes; the monkey was again subjected to the action of the sun, this time for one hour and twenty-four minutes. At 3.20 in the afternoon it had a respite from the sun of seven minutes and was afterward in the sun for forty-eight minutes, until 4.15 in the afternoon. This makes it probable that on this day the monkey was exposed to the Manila sun for about seven and one-half hours, including the hottest portion of the day.

The monkey showed no symptoms of distress from the action of the sun, although exposed for seven hours. It did, however, show some depression, as it lay on the pole for short periods in the more severe portions of the day. No sign of injury was noticed on this day or on any succeeding day.

*The effect of the sun on the monkey's temperature.*—Although the monkey showed no distress from this long exposure to the

<sup>4</sup> *Trans. Roy. Soc. Edin.* (1906), 45, I, 65-104. The maximum normal temperature of *Rhesus macacus* observed by Eyre and Kennedy was 40°. *Journ. Physiol.* (1907), 36, xxx-xxxii.

sun, yet there was a distinct measureable effect produced. Table II shows the effect of the sun upon this monkey as indicated by body temperature.

TABLE II.—*Effect of sun upon monkey's temperature. Monkey 4 in the sun, 1 meter above the ground, November 29, 1911.*

Time.	Air temperature. °C.	Body temperature. °C.	Time. a. m.	Black-bulb reading. °C.	Wind. Meters per second. P. et.	Relative humidity.	Remarks.
a. m.							
8.10	25	38					In animal house.
8.86	28						Exposed to sun at 8.35 a. m.
9.28	29	39.7	9.00	448.2	0.0	59.0	After 55 minutes' exposure. No distress symptoms.
10.25	30	40.8	10.00	451.7	2.0	56.0	
11.25	30.2	39.5	{ 11.00 12.00	{ 47.7 47.8	{ 3.0 8.5	{ 56.0 55.0	No distress symptoms. Do.
p. m.							
1.15	32	39.4	1.00	450.9	4.0	51.5	Do.
2.15	32	40.0	2.00	50.0	0.0	48.0	8 minutes of cloud (1.47-1.55), no distress symptoms.
3.20	31	39.6	3.00	447.2	3.0	46.0	No distress symptoms.
4.15	30	39.4	4.00	44.4	0.0	50.0	7 minutes of cloud (3.20-3.27), no distress symptoms.

\* The air temperature here given was that registered by an ordinary chemical thermometer hanging in the sun near the monkey.

† Time of Weather Bureau observation.

‡ Wind velocity in meters per second.

§ Interpolations. Since the black-bulb readings at the Weather Bureau are taken at relatively infrequent intervals, a method of obtaining interpolations recommended by the Weather Bureau authorities was adopted. It is as follows:

"Find the difference between black-bulb readings and the corresponding readings of the Violette actinometer. Interpolate as many means between these differences as there are observation times between the black-bulb readings. Subtract or add these means as the case demands to the corresponding Violette readings to get the black-bulb interpolations."

The method is illustrated by the following table:

Time.	Black-bulb.	Violette.	Difference.	Mean.
a. m.	°C.	°C.	°C.	°C.
8.00	42.5	58.0	-10.5	
9.00	(48.2)	59.0		-10.76
10.00	(51.7)	62.7		-11.02
11.00	47.7	59.0	-11.3	
12.00	(47.8)	59.5		-11.2
p. m.				
1.00	(50.9)	62.0		-11.1
2.00	(50.0)	61.0	-11.0	
3.00	(47.2)	60.0		-12.8
4.00	(44.4)	59.0		14.6
- 5.00	27.6	44.0	-16.4	

\* The interpolations are inclosed in parentheses.

Table II shows that the temperature of the monkey did not rise above 40.8° on seven hours' exposure to the sun. This was rather surprising in view of Aron's statement, and is all the more noteworthy in view of the fact that on this day the monkey, being still wild, struggled hard every time the temperature was taken. On comparing the conditions at 10.25 in the forenoon on November 29 with the conditions at 3.40 in the afternoon on November 28, it is seen that the air temperatures were the same on the two occasions, while the body temperature was 1.5° higher in the sun than in the shade. This difference might be taken for a measure of the effect of the sun's rays, if we did not know that the monkey's temperature depends also upon the air humidity, wind velocity, and individual resistance, factors apparently overlooked by Aron in the statements cited.

Weather data for these two days are given in Table III in a form convenient for comparison. A study of the table will give an idea of the action of the sun's rays alone.

TABLE III.—*Action of the sun's rays alone on monkey 4.*

Exposure.	Date.	Time.	Body temper- ature. °C.	Time.	Air temper- ature. °C.	Weather.			
						a. m.	p. m.	Black- bulb read- ing. °C.	
Sun.....	Nov. 29	10.25	40.8		10.00	28.8	51.7	2.0	56
Shade .....	Nov. 28	3.40	39.8		8.00	30.0	shade	1.0	56
					4.00	29.5	shade	0.0	59

When we compare the air temperatures, winds, and humidities of these two periods of observation, we find that, when the monkey was in the sun, the air temperature and humidity were less and the wind was greater than when it was in the shade. Each of these factors—the lower air temperature, the lower humidity, and the stronger wind—would tend to produce a lower temperature in the monkey. Since this was the first exposure to heat in the sun, the power of resistance of the monkey to the sun and heat was probably about the same as on the day previous in the shade. The sun's rays, therefore, are the only factor that would tend to raise the temperature of the monkey above that of the previous day when the monkey was in the shade. There-

fore it seems reasonable to suppose that the increase of  $1.5^{\circ}$  in body temperature over that of the day before in the shade was due to the sun's rays alone. Since the black-bulb thermometer reading, when the monkey's temperature was raised by the sun's rays, was  $51.7^{\circ}$ , and since the air temperature was lower at this time, the humidity probably lower, and the wind higher, it would appear that the sun's rays which were strong enough to produce a black-bulb reading of  $51.7^{\circ}$  were more than strong enough at this time to raise this monkey's body temperature through  $1.5^{\circ}\text{C}$ .

*The effect of conditions other than the sun's rays and air temperature upon this monkey.*—Table II further shows that the body temperature of this monkey in the sun was higher when the air temperature was only  $30^{\circ}$  (10.25 in the morning) than when the air temperature was  $32^{\circ}$  (1.15 or 2.15 in the afternoon). This emphasizes the well-known fact that the hottest weather is not necessarily the most injurious, unless we understand by "hottest" something else than the highest temperature registered by the ordinary thermometer, that is, the atmospheric temperature. If we compare the weather conditions at 10.00 o'clock in the morning, which were soon followed by the highest body temperature observed on this day, with those obtaining at 1.00 in the afternoon, which were closely followed by a body temperature  $1.4^{\circ}$  lower, we find that this lower body temperature, in spite of a higher air temperature, was accompanied by a lower reading of the black-bulb thermometer, a higher wind velocity, and a lower relative humidity. Each of the last three conditions would work toward offsetting the effect of increased air temperature, and this fact accounts, at least partially, for the lower body temperature when the surrounding air was  $2^{\circ}$  hotter. These observations show why the portion of the day that was the hottest, judged by the ordinary thermometer, was not the most injurious to the monkey; it was because the energy of the sun's rays was less, the wind was blowing harder, and the air was not so humid. Therefore there are four factors that must always be taken into account in any attempt to determine the cause of a rise in body temperature or of death following exposure to the sun, namely, the energy of the sun's rays and the temperature, the movement, and the humidity of the air.

*The relation of heat to the death of monkeys in the sun.*—Since Aron makes the statement that monkeys die in "seventy to eighty

minutes" when exposed to the Manila sun, even in the coolest portion of the year,<sup>a</sup> and since this monkey did not die, though exposed to the Manila sun for seven hours and twenty-four minutes, it might be inferred that this day happened to be exceptionally cool, much cooler than the days on which Aron's monkeys died. On comparing the Weather Bureau records for these days, however, the energy of the sun rays, to which this monkey was exposed, was greater and the surrounding atmosphere was hotter than those to which Aron's monkeys were exposed. The air temperature and the black-bulb readings are given in Table IV.

TABLE IV.—*Relation of sun's rays and atmospheric temperature to the death of monkeys in the sun.*

Monkey No.	Date.	Maximum black-bulb. <sup>a</sup>	Air temperature.	Authority.	Duration of exposures.	Result.
2	1910. Nov. 16 1911.	°C. 51.8	°C. 30.8	Aron <sup>b</sup> .....	H. m. 0 38	Death.
11	Jan. 18	43.3	29.8	....dob.....	1 50	Do.
12	Jan. 18	47.3	30.3	....dob.....	0 40	Do.
18	Jan. 26	42.4	28.8	....dob.....	1 0	Do.
4	Nov. 29	51.7	28.8-31.2	Shaklee.....	7 24	No distress.

<sup>a</sup> Interpolations. For method, see footnote to Table II.

<sup>b</sup> Aron, op. cit., p. 111.

<sup>c</sup> Number 12 was shaved.

<sup>d</sup> Aron, op. cit., p. 114.

From Table IV one might draw the conclusion that the energy of the sun's rays is a relatively small factor among those that combine to produce the monkey's death. It is seen from the table that one monkey remained in the sun seven hours and twenty-four minutes without any signs of distress and that four other monkeys in the sun at the same temperature, or a lower one, and in sun rays of equal or less energy, died in thirty-eight, one hundred ten, forty, and sixty minutes, respectively. This further emphasizes the importance of the conditions other than the temperature of the atmosphere or energy of the sun's rays which act upon the monkeys exposed in the way in which Aron exposed his monkeys. The data given in Table V shows this more clearly.

<sup>a</sup> Aron, *This Journal, Sec. B* (1911), 6, 110.

TABLE V.—*Relation of heat from the ground,<sup>a</sup> of the wind, and of humidity to the monkey's death in the sun.*

Monkey of—	Date.	Time of death.	Time of weather observation.	Black-bulb.	Wind. <sup>b</sup>	Relative humidity.	Duration of exposure.	Remarks.
Aron:								
2.....	1910.	a. m.	a. m.	°C.	M. s.	P. ct.	H. m.	
	Oct. 16	10.08	10.00	51.8	0 0	69	0 38	On hot surface.
	1911.	p. m.	p. m.					
11.....	Jan. 18	4.15	4.00	48.3	3 0	63	1 50	Do.
b12.....	Jan. 18	8.10	8.00	47.8	3 5	61	0 45	Do.
18.....	Jan. 26	a. m.	a. m.					
		11.50	12.00	42.4	3 5	66	1 0	Do.
Shaklee:								
4.....	Nov. 29	.....	10.00	51.7	2 0	55.0	1 25	Not on hot surface.
			p. m.					
4 (continued).			1.00	50.9	4 0	51.5	4 25	Do.
4 (concluded).		Lived	4.00	44.4	0 0	50.0	7 15	Do.

<sup>a</sup> Heat from ground is not shown in this table.<sup>b</sup> No. 12 was shaved.

c Velocity in meters per second.

NOTE: Reports for monkeys 2, 11, and 12 were taken from page 111 of Aron's paper, and for monkey 18 from page 114 of the same paper.

It will be seen from Table V that the heat from the sun's rays as indicated by the black-bulb thermometer was considerably greater in the case of the monkey that lived than in the cases of three that died. Therefore it cannot be said that the sun's rays killed Aron's monkeys. The wind conditions were as favorable to the monkeys that died, but the humidity of the air surrounding the monkeys that died was much greater. There is another important factor in the death of Aron's monkeys which must not be overlooked. His monkeys rested on the ground or roof. The ground and roofs become very hot in a hot sun. It seems possible that the heat which the monkey's body received from the hot roof or from the ground may have far exceeded that absorbed from the sun's rays.

Since the sun's rays combined with the other weather conditions produced so little effect upon monkey 4, in absence of the heat from the ground, it was decided to place the monkey on the ground, to determine the influence of the heat from the ground.

*The effect of the combined action of the sun and the heat radiated and conducted from the ground.*—On Friday, December

1, the monkey was placed on the tennis court chained to a small scantling, 6.5 by 7.5 centimeters, that was lying on the ground. He was free to move about and to sit on the scantling, which would not be so hot and which would raise him about 6.5 centimeters above the ground. He was put out at 8.25 in the forenoon. This day was also a bright day. The Weather Bureau records show seven hours and eighteen minutes of sunshine. Taking these records again as a basis for our estimate, he was exposed to the sun and hot ground from 8.25 until 11.01 (two hours and twenty-four minutes), from 11.25 to 11.45, and from 12.05 to 2.45 (two hours and twenty-eight minutes). Table VI shows the effects of these conditions upon the monkey's temperature.

TABLE VI.—*Combined action of sun and hot ground on the monkey. Monkey 4, in the sun and on the ground, December 1, 1911.*

Time.	Air temperature.*			Body temperature.	Remarks.
	On ground.	8.5 cm. above ground.	1 m. above ground.		
7.55			22.5	37.4	Shade (in the house).
8.25					Exposure began, sun.
9.43	38	32	28.5	39.8	Sunshine. <sup>b</sup>
10.55	42	32.5	29	39.4	Do. <sup>b</sup>
1.17	46	35	32	40.5	Do. <sup>b</sup>
2.30	44.5	35	32.5	41.7	Do. <sup>b</sup>
3.15	37.5	30.5	29	42.0	Cloud. <sup>b</sup>
4.00	34	29.5	29	39.0	Do. <sup>b</sup>

\* Air temperature as indicated by chemical thermometers kept in the sun in the positions indicated—namely, on the ground, 8.5 centimeters above the ground, and 1 meter above the ground.

<sup>b</sup> Sunshine and cloud as recorded at the Weather Bureau, 0.8 kilometer away.

It will be seen from Table VI that the combined action of the sun and the hot ground for two hours and twenty minutes in the forenoon (8.25–10.55) did not raise the temperature of this monkey above its maximum normal. If monkeys "die in seventy to eighty minutes" when placed on the ground in the Manila sun, this monkey had already acquired a marked increase in powers of resistance; but since not all days are alike, even in Manila, it is necessary to study the meteorological conditions before drawing a conclusion. On December 1, the day of the exposure under consideration, the conditions seemed to be as severe as those obtaining when some of Aron's monkeys died. This is brought out by a comparison of Table VII with Table V.

TABLE VII.—*Weather conditions on December 1, 1911 (at Weather Bureau, 0.3 kilometer away).*

Time.	Black-bulb reading. °C.	Wind. M. s.	Relative humidity. °C.	Sunshine (heliograph reading).
a. m.				
8.00	40.5			
9.00	*45.8	0 0	62.0	7.31-11.01
10.00	*47.8	2 5	60.0	
11.00	48.3	5 0	59.0	
12.00	*46.7	3 0	54.0	11.25-11.46 11.46-11.47
p. m.				
1.00	*51.7	0 5	58.0	12.05- 2.45
2.00	50.0	1 5	58.0	
3.00	*49.8	0 0	50.0	
4.00	*36.1	2 0	68.0	8.58- 4.10

\* Interpolations, see Table II, footnote.

From a comparison of these two tables it seems probable that at 9 o'clock and at 10 o'clock in the forenoon and at 1 o'clock in the afternoon on December 1 the conditions to which monkey 4 was subjected were as severe as those that produced the deaths of monkeys 11 and 13 of Aron's series. If this be the case, the few exposures of monkey 4 had already developed in it a greatly increased capacity for resisting the evil influences of the exposure to the tropical sun under the conditions named. And although it is probable that the wounds in Aron's monkeys reduced their resistance and that Aron's monkeys struggled more because of the insertion of the thermocouple into these inflamed wounds, it seems justifiable to draw the conclusion that No. 4 had already acquired considerable increase in its powers of resistance, especially when it is remembered that it showed no distress at all on this day, nor did it show on the following days any evidences of having received any injury from this exposure. Another possibility is that this monkey was an especially resistant monkey. This does not seem probable, because similar results were obtained with all the monkeys studied in this series as is brought out below.

*The progress and degree of acclimatization.*—The results of this day's exposure gave me more hope of being able to learn, by the use of the monkey, something about acclimatization, if not to the sun's rays, at least to the combination of all the climatic factors, including the heat from the ground.

Exposures of this monkey were made on every sunny day thereafter, except holidays, for five months. All the later ex-

posures were made on the black asphalt roof of the laboratory. On the first days, during the exposures, the monkey was chained to a scantling which rested upon the roof, but in the last and hottest months it was chained to a wire, so that it rested directly upon the roof. Table VIII, which gives the highest daily maximum temperatures observed in this monkey in the five months, brings out the progress and degree of acclimatization of this monkey to the combined meteorological factors plus the intense heat from the roof—in other words, to the Manila climate at its worst.

TABLE VIII.—*Highest daily maximal body temperatures. Acclimatization (monkey 4 kept in the sun and in contact with the heated roof).*

1911.	°C.
December 1	42.0
December 6, 15	40.5
December 7	40.0
December 12	40.0
December 18	40.0
Average *	40.6
December 20	38.5
December 21	39.8
December 22	39.4
December 27	39.3
December 29	39.9
Average	39.6
1912.	
January 3	39.7
January 5, 11, 16	39.5
January 17	39.9
January 26	39.9
January 29	39.9
Average	39.8
February 9	39.5
February 10, 13	39.4
February 12, 27	39.3
February 14	39.6
February 29	39.2
Average	39.4
March 1	39.6
March 5	39.5

\* Average of five highest maxima.

TABLE VIII.—*Highest daily maximal body temperatures. Acclimatization (monkey 4 kept in the sun and in contact with the heated roof)*—Cont'd.

1912.	°C.
March 12	39.4
March 16	39.8
March 30	39.5
<b>Average</b>	<b>39.6</b>
April <sup>b</sup> 10, 11	39.5
April 12, 16	39.5
April 18	39.9
April 22	39.5
April 26	40.1
<b>Average</b>	<b>39.7</b>

<sup>b</sup> During April the required hours for civil service employees were from 7.30 in the forenoon to 12.30 in the afternoon; hence the monkeys were not usually exposed much beyond noon in this month. Only on days that were expected to be very hot were the monkeys kept out in the afternoon. More will be said about this later.

It will be seen from Table VIII: (1) That never after December 1, the first day on the ground, was the temperature of the monkey found above 40.5°—that is, the combined action of the hot sun and hot roof on the hottest days did not produce as much response in the monkey as did the sun's rays alone on November 29, 1911 (a body temperature of 40.5° apparently produces no discomfort in the acclimatized monkey); (2) that never but once after December 15, the ninth day on the ground, did the temperature exceed 40°, which is a temperature but little, if any, above the maximal shade temperature of this monkey; (3) that the monkey's temperature never exceeded the maximal shade temperature in February and but once, if at all, in March, and but twice in April, the record hot month. This seems to make it clear that a great deal of the acclimatization took place in the first two days of exposure, November 29 and December 1, that by December 18, the eleventh day on the ground, a rather high degree of resistance had been acquired, and that by the end of the second month the resistance had probably reached its maximum. It also seems to show that the temperature of a thoroughly acclimatized monkey, exposed day after day to the sun in contact with a hot roof, rarely exceeds its maximal normal temperature.

The history of the monkey thus far indicates in a decisive manner, when the earlier history is compared with the later and when it is compared with the experiments of Aron: (1) That

there is a marked difference in the effects of the climate of Manila on different days; (2) that the maximal normal temperature of this monkey is probably not below  $39.5^{\circ}$ ; (3) that this monkey had acquired increased power of resistance to the tropical climate at its worst; (4) that the acclimatization was probably most rapid in the first two days; (5) that the acclimatization probably did not approximate completion much before the end of two months' exposure; (6) that an acclimatized monkey may show no discomfort in the sun of Manila even when sitting on the hot roof during the hottest days of the year; (7) that the temperature of an acclimatized monkey sitting on a bare, hot asphalt roof day after day in the hottest portions of the year in Manila may not rise above its maximal normal temperature ( $39.9^{\circ}$ ) oftener than once or twice a month; and (8) that the sun's rays alone probably have no injurious effect upon the monkey.

#### ACCLIMATIZED MONKEYS COMPARED WITH UNACCLIMATIZED

Although the comparison of the behavior of monkey 4 in the sun with the behavior of the monkeys studied by Aron seems to prove the acquirement of greatly increased resistance by the former, the data were too few to be conclusive, and it was necessary to expose it and other monkeys that had been exposed to the sun alongside of monkeys that had not been so exposed. Table IX gives the results of exposure to the sun and in contact with roofs of acclimatized monkeys alongside of unacclimatized.

It is readily seen from the facts shown in Table IX: (1) that the unacclimatized monkeys placed in the sun in contact with the hot roof may die in from forty minutes to six hours, depending upon the individual resistance and upon the climatic factors obtaining; (2) that ten exposures to the sun produced greatly increased resistance to the sun, but were not always sufficient to produce thorough acclimatization; (3) that twenty-one exposures produced a high degree of immunity if not thorough acclimatization; (4) that the temperature of an acclimatized monkey rarely exceeds the maximum normal temperature, even when exposed to the combined action of the sun and the hot roof; (5) that sickness reduces the resistance to heat or to heat combined with other climatic factors (see monkey 14, April 26); (6) that exposure in contact with the hot ground or roof may prove rapidly fatal when exposure 1 meter above the roof produces no symptoms (see monkeys 16 and 19, March 8 and 12), that is, much the greater portion of the injury to monkeys exposed as Aron exposed them seems to be due to the heat from the roof rather than to the sun's rays.

TABLE IX.—Effect of the sun and a hot roof on acclimatized and on unacclimatized monkeys exposed simultaneously under the same conditions.

Date.	Acclimatized.				Unacclimatized.				Remarks.
	Monkey.	Exposures.	Dura-tion of last expo-sure.	Result, body tem-perature.	Monkey.	Exposures.	Dura-tion of last expo-sure.	Result.	
Dec. 29, 1911			H. m.	°C.			H. m.		
	4	21	7 20	39.9	7	9	46 0	Death .....	Time not exact. 1 meter a- bove roof. Contact with roof. (cont.)
					8	1	1 28	do .....	
					9	1	1 1	do .....	
					10	1	1 56	do .....	
					11	1	1 42	do .....	
	4	75	7 15	39.1	16	1	4 55	(a)	
	12	43	7 15	40.7					
	13	43	7 15	39.95					
	14	41	7 15	39.2	16	1	0 40	Death .....	
Mar. 8, 1912									
	15	41	7 15	39.8					
	4	77	6 45	39.3					
	12	45	6 45	39.6					
	13	45	6 45	40.6	18	4	4 0	do .....	
	14	43	6 45	39.5					
	15	43	6 45	39.8					
	4	78	7 15	39.4					
	12	46	7 15	39.5	19	3	2 45	(b)	
	13	46	7 15	39.8	c 19	.....	0 47	Death .....	
Mar. 11, 1912	14	44	7 15	39.8					1 meter a- bove roof. Contact with roof.
	15	44	7 15	39.5					
	4	92	7 10	39.0					
	12	60	7 10	39.2					
	13	60	7 10	39.2	23	1	0 40	do .....	
	14	58	7 10	39.5					
	15	58	7 10	40.1					
	4	93	7 15	38.8					
	12	61	7 15	39.0					
	13	61	7 15	39.2	17	2	0 45	(?)	
Mar. 29, 1912	14	59	7 15	38.7					1 meter a- bove roof. Contact with roof.
	15	59	7 15	38.8					
	4	110	7 15	40.1					
	12	81	7 15	39.6	20	46	1 33	Death .....	
	13	81	7 15	40.0	21	46	1 17	do .....	
	14	*79	7 15	(?)	22	10	5 9	do .....	
	15	79	7 15	40.0					
April 26, 1912									

\* Body temperature, 39.6°.

b Body temperature, 41° and 39.8°.

c Continuation of experiment with monkey 19.

d Some of these exposures were 1 meter above the roof.

e Monkey 14 had been sick for the last few days.

f Died in 4 hours and 37 minutes.

*Nature of this acclimatization.*—In this research facts have been brought out that give some information as to the nature of the acclimatization produced.

First, acclimatized monkeys sweat much more than unacclimatized monkeys when placed on a hot surface in the sun. Aron<sup>\*</sup> had stated that monkeys have no sweat glands and I, not having had occasion better to inform myself on this point, was greatly surprised soon after I had begun these experiments on acclimatization to notice, while watching a monkey in the sun, small beads of sweat glistening in the hair of its forehead. After this I made systematic examinations of the surfaces of the monkeys' bodies in order to get some idea of the amount of sweating. I regularly found beads of sweat on the heads of acclimatized monkeys placed on the roof in the sun, if the roof was very hot. Sweat was found on the backs of the monkeys also, being greater in quantity on the upper back and gradually diminishing in quantity toward the tail. At the root of the tail comparatively little sweat was found. The palms were frequently found wet with sweat, and they often left wet imprints when lifted from the surface of the asphalt roof. On other parts of the body I found very little sweat. On some parts I did not succeed in finding any, but since the skin seems everywhere provided with well-developed sweat glands, it seems probable that there was insensible perspiration over the areas that did not show visible sweat. I found, therefore, that the acclimatized monkey sweats a good deal while resting on a hot roof in the sun. On the contrary, I found that the unacclimatized monkey sweats very little, if at all, under like conditions. This difference in perspiring between acclimatized and unacclimatized monkeys was very striking, so striking that one might be justified in inferring that it was because of this difference in sweating that the body temperature of the acclimatized monkey, under conditions that cause a rapid and fatal rise in the body temperature of the unacclimatized, does not rise above the maximum normal.

Secondly, it was found that a small dose of atropin sulphate caused a marked rise in the body temperature of an acclimatized monkey exposed to a hot sun. Atropin has been found to diminish the action of sweat glands by depressing the secretomotor nerve endings in the glands and so preventing nerve impulses from stimulating the secretory cells. Each time that I injected a small dose of atropin sulphate under the skin of an acclimatized

\* Aron, op. cit., p. 110.

monkey resting on the roof in a hot sun, the sweating decreased and the body temperature began to rise almost immediately and soon reached such a dangerous height that it was deemed necessary to remove the animal to the shade to prevent prostration and death from heat stroke. A like dose of atropin produced no change in the body temperature of monkeys in the shade. In fact, after such doses given to monkeys in the shade, I saw no marked symptoms of any sort. These experiments with atropin strongly support the inference already drawn that the difference in the amount of perspiring in acclimatized and unacclimatized monkeys is enough to account for the fact that unacclimatized monkeys die of heat stroke under conditions that do not raise the temperatures of acclimatized monkeys above the normal.

Thirdly, it was observed that when the relative humidity of the atmosphere was much higher the tendency to rise of the body temperature of an acclimatized monkey in the sun on the roof was markedly greater. Since an increase in relative humidity has a tendency to raise the body temperature by diminishing the rate of evaporation of water from the surfaces of the body, this supports the inference that it was the sweating of the acclimatized monkey which caused its temperature to remain normal under circumstances that killed the unacclimatized monkey with heat stroke.

Fourthly, attempts to acclimatize rabbits failed signally. The methods that had proved successful in acclimatization of monkeys were tried with rabbits. Rabbits were carefully exposed to the sun day after day, being removed to the shade as soon as they seemed approaching danger of heat prostration. The rabbits remained in good condition, but no increase in resistance to the action of the heat could be detected. On succeeding days the period of exposure could not be appreciably lengthened with safety to the animal. Rabbits that had been submitted to this process of acclimatization for many days in succession were exposed alongside of rabbits that had not been previously exposed. I was not able to detect any difference in the powers of resistance between the rabbits that had been submitted to the acclimatizing process and those that had not been previously exposed. The rabbits that had been submitted became prostrated as soon after insolation as the unexposed and died as soon. Rabbits are not known to perspire. Here there was no perspiring to be increased, and no acclimatization resulted. This fact, therefore, also gives indirectly some support to the infer-

ence that the acclimatization observed in the case of the monkey consisted in the development of increased capacity for sweating under the conditions of the experiment.

*Mechanism of this acclimatization.*—It remains to inquire how this increased sweating observed in acclimatized monkeys was brought about. It followed upon simple exposure to the sun, which means exposure to heat and light rays. The increase in sweating occurred upon the surfaces most exposed to the heat, namely, the palms of the hands, which came in contact with the hot roof, and the back, which was uniformly turned toward the sun. The primary effects of the heat upon the monkey were, first, the elevation of the temperature of that portion of the skin which was exposed to the heat rays, including, among other structures there found, the sensory nerve endings, the secretory cells, and the secretomotor nerve endings in the sweat glands; secondly, the elevation of the temperature of the entire body, most marked in the first few days of exposure. A secondary effect evidently was an increase in sensitiveness of one or more parts of the sweating mechanism, which increase was more or less persistant. Since a small dose of atropin stops the sweating in an acclimatized monkey, presumably by paralyzing the secretomotor nerve endings in the sweat glands, the increase in sensitiveness must lie in the nervous mechanism and not in the secretory cells of the sweat glands. The three portions of this nervous mechanism which seem most likely to be affected are the sensory heat nerve endings, the secretomotor nerve endings in the sweat glands, and the nerve cells concerned with temperature regulation. The endings mentioned would be most affected by the direct heating of the skin. The cells could be affected in two ways: First, by the arrival of a greater number and of stronger impulses, coming from the highly heated skin, and secondly, by being heated above their normal temperature by the increase in body temperature. Since, when stronger and more frequent impulses pass into a given tract of the brain, the brain becomes so changed that stimuli to this tract set up greater responses than before, it does not seem unreasonable to suppose that the nervous mechanism regulating body temperature, excited by the unusually strong heating of the skin, may become so changed that any nerve impulses coming to it will produce greater discharges than before. It may then be justifiable to assume that the acclimatization observed in these experiments consisted, at least in part, in a sensitization of nerve cells concerned with temperature regulation of which cells those con-

cerned with the stimulation of the sweat glands seem to be especially affected.

However, it must not be forgotten in this connection that there may have been other conditions operating to raise the resistance of these monkeys to heat. For example, the change in diet to which each monkey was subjected when it was placed under observation may have aided in increasing its resistance. Observations by the author in connection with experiments on man indicate that in man some diets lower the resistance to heat and others raise it. Whether or not the change in the monkey's diet was sufficient to affect its resistance remains to be ascertained. The fact that monkeys, partially acclimatized, kept in the shade on the same light diet, seemed to loose in powers of resistance indicates that the diet here plays a minor rôle.

*The significance of this acclimatization of monkeys for the acclimatization of man.*—Since a moderate ability to sweat and a light, suitable diet are sufficient to render the monkey practically immune to the worst combinations of weather conditions that occur in a tropical region such as that in which Manila lies, it would seem that man might readily be acclimatized to the same conditions. There are many facts that point in this direction. Man seems in every way better adapted than the monkey to resist the tropical climate. The monkey is ordinarily easily killed by heat stroke as has been shown by the experiments of Aron and by the experiments here reported. It may be, as Aron stated, that the monkey is less resistant to the worst combinations of tropical weather than the white man. The temperature-regulating mechanism in man is much more sensitive than that in the monkey, as shown by the smallness of the normal variation of body temperature in man as compared with that in the monkey. The sweating mechanism in man has many times the capacity of that in the monkey, and as the temperature of the surrounding atmosphere approaches the temperature of the body, this becomes the most important means of eliminating heat from the body. The internal heat production of man on a light diet is smaller in proportion to body surface than that of the monkeys subjected to this experiment. Man stands higher above the hot surface upon which he rests or moves; hence he would receive less heat from the ground and be subjected to a more rapid movement of air over the body surface than would the monkey. Man's body has much less hair than the monkey's; hence the escape of heat from his body by radiation, conduction, or evaporation is less interfered

with. Man can so select and arrange his clothing that it will interfere little with the escape of heat from the body, while at the same time it will shield the body from the heat rays coming from the sun. Moreover man is acquainted with a larger variety of foods. This enables him to avoid the useless production of heat and toxins in the body. By taking at each meal only enough of each food to furnish the quantity of each element and each compound needed by the body at the time, he avoids for his body the necessity of burning an excess of any one food in order to get a sufficient quantity of some one of its constituents; he also avoids leaving a large or dangerous residue in the intestine, thus avoiding or diminishing the elaboration of poison in the intestine by bacteria.

*Experimental acclimatization of the white man to the tropics.*—The foregoing observations by me on the acclimatization of the monkey to the injurious combinations of climatic factors that may arise in the tropics led me to institute some experiments on the white man to see whether or not the inference in regard to man could be experimentally justified. The experiments were begun upon me—a blonde American—and have already continued for a period of six months. As far as the experiments have gone, they have justified in every particular the inference drawn. I now frequently walk at a rapid, forced pace, bare-headed in the Manila sun at midday for more than an hour at a time, without causing more serious symptoms than a moderately abundant perspiration. At no time were more serious symptoms observed than a mild erythema solare, resulting in moderate desquamation of epidermis and some increase in tan. At no time was there any sign of a deficiency in sweating, nor was there ever any indication that the necessary amount of sweating was at all exhausting.

It was noted, however, that changes in diet produced marked changes in the power of resistance. Since diet has such a marked influence and since the white man sweats much more readily than the monkey, it seems that the major factor in the acclimatization of the white man is not the development of his capacity for sweating, but rather the proper regulation of diet. There are other factors of more or less importance for the white man, for instance, the development of tan on the portions of the body exposed to the sun.

*Duration of this immunity acquired by monkeys.*—A few experiments seemed to indicate that acclimatized monkeys lose their resistance if they are kept in the shade for a few days.

I hope to make a more detailed report of these experiments in a subsequent paper.

#### SUMMARY

1. The normal temperature of the Philippine monkey probably varies between 37.5° and 39.5° C.
2. Unacclimatized Philippine monkeys (*genus Pithecius*) exposed to the sun in Manila live or die of heat stroke in the course of from several minutes to several hours, depending upon the conditions.
3. The conditions making for a rapid death are: A hot sun; proximity of a large, hot surface, such as the ground or a roof; high relative humidity of the atmosphere; and a low wind velocity.
4. The death under these conditions is due to an accumulation of heat in the body.
5. The lack of any one of the above conditions may prevent death.
6. The effect of the sun's rays alone on this monkey is comparatively slight.
7. These monkeys on a suitable diet become acclimatized to the conditions mentioned, if exposure to the conditions is gradual.
8. A small dose of atropin will cause the death of an acclimatized monkey by stopping the perspiration.
9. The acclimatization consists in an increase in the sensitiveness of the nervous mechanism which regulates the body temperature. The increase in sensitiveness produces an increase in the rate of perspiration under the conditions named above, producing in this way what may be termed an immunity.
10. This immunity is readily lost if the monkeys are kept in the shade.
11. Some forms of sickness diminish the powers of resistance to the above-mentioned conditions.
12. Some toxins produced in the intestine lower this resistance.
13. Rabbits showed no increase in resistance when treated in the manner used to acclimatize monkeys.
14. Healthy white men may be readily acclimatized to the conditions named, that is, to the tropical climate at its worst.
15. The amount of sweating necessary to keep the body temperature of a healthy white man from rising above normal is not excessive, even when the man is doing considerable physical work in the midday sun in such a tropical climate as that which obtains at Manila, provided the man has been sufficiently long

on a suitable diet and introduces himself gradually into the work in the sun.

16. In the acclimatization of the white man the most important factor is the proper regulation of the diet.

17. The effects from the tropical sun seemed to be exactly the same as the effects from the sun in the United States; that is, no effects were seen or felt in these experiments that were different from what would have been expected under like circumstances in the northern portion of the United States.

# THE INFLUENCE OF BILE UPON THE DISTRIBUTION OF CHOLERA VIBRIOS IN THE DIGESTIVE SYSTEM OF EXPERIMENTAL CHOLERA CARRIERS<sup>1</sup>

By OTTO SCHÖBL

(From the Biological Laboratory, Bureau of Science, Manila)

The distribution of cholera vibrios in the alimentary canal of experimental cholera carriers has been studied in the early experiments.<sup>2</sup> It was found that the excretion of cholera vibrios in the fæces of successfully infected animals is irregular and not as frequent as one would expect. Out of 26 samples of fæces taken from 26 guinea pigs, only 2 were found to contain cholera vibrios at the time of examination. In another experiment a systematic examination of fæces for the presence of cholera vibrios was made in 18 guinea pigs. Out of 71 examinations of fæces taken from these animals at various times, only 14 tests were positive.

During the studies on the influence of bile upon the state of cholera carriers in experimental animals,<sup>3</sup> it was discovered accidentally that animals fed on bile excreted cholera vibrios in their fæces more frequently than normal cholera carriers. This finding was considered important enough to be further studied.

A series of guinea pigs was infected by intravesicular injection. Some of the animals were fed on bile; the remainder were kept as normal controls. They were killed and examined for the presence of cholera vibrios at intervals. Cultures were made from the gall bladder, duodenum, ileum, cæcum, and fæces. Both direct Dieudonné's plate and peptone cultures were planted.<sup>4</sup>

<sup>1</sup> Received for publication October 5, 1916.

<sup>2</sup> *Journ. Inf. Dis.* (1916), 18, 307-314; (1916), 19, 145-152.

<sup>3</sup> *This Journal, Sec. B* (1916), 11, 157.

<sup>4</sup> For details of technic, see *Journ. Inf. Dis.* (1916), 18, 307-314.

TABLE I.—*Showing the influence of feeding bile upon the distribution of cholera vibrios in the alimentary canal of experimental cholera carriers as compared with that of normal cholera carriers.*

[+, cholera vibrios found; —, cholera vibrios not found; v. f., very few, less than 6 colonies; f., few, about 12 colonies; n., numerous, about 200 colonies; v. n., very numerous, more than 200 colonies.]

CARRIERS: RECEIVED OX BILE PER OS.

Guinea pig.	Examined, days after inoculation.	Direct plates.				Peptone cultures.			
		Bile.	Duo- denum.	Ileum.	Cae- cum.	Gall blad- der.	Duo- denum.	Ileum.	Cae- cum.
1.....	8	v. n.	v. n.	v. n.	n.	+	+	+	+
2.....	8	n.	n.	v. n.	f.	+	+	+	+
3.....	9	n.	n.	v. n.	n.	+	+	+	+
4.....	9	v. n.	n.	v. n.	f.	—	+	+	+
5.....	10	v. n.	v. n.	v. n.	n.	+	+	+	+
6.....	12	v. n.	v. n.	v. n.	v. n.	+	+	+	+

CONTROL CARRIERS: RECEIVED NO OX BILE.

7.....	8	n.	v. f.	f.	v. f.	+	+	+	+
8.....	9	n.	v. f.	v. f.	—	+	+	+	+
9.....	9	n.	v. f.	v. f.	—	+	+	—	—
10.....	10	v. n.	v. n.	v. n.	f.	+	+	+	—
11.....	12	v. f.	—	v. f.	—	+	—	—	—

These experiments show that the distribution of cholera vibrios in the alimentary canal of experimental cholera carriers fed on ox bile was more extensive, the elimination of cholera vibrios in the faeces was more constant, and the cholera vibrios were present in the alimentary canal in larger numbers than in the case of the carriers that received no bile.

## COMMON INTESTINAL PARASITES

By FAUSTINO GARCIA

(From the Southern Islands Hospital, Cebu, P. I.)

To obtain an idea of the prevalence of infection by intestinal parasites among Filipinos in the Visayan Islands of the Philippine Islands, the records of stool examinations from April, 1913, when the Southern Islands Hospital was established, to November, 1916, were examined. For these three and a half years the stools of 1,603 patients were submitted to routine examination. The majority of the patients were of the lower classes, so that my statistics represent more or less the common Filipino people residing in the Visayan Islands and especially in Cebu Island.

Table I gives the names of the intestinal parasites and the percentages of infections by the common intestinal parasites among the Filipinos whose stools were examined.

TABLE I.—*Percentages of infections by the common intestinal parasites among Filipinos examined.*

	Number.	Percent.
Patients examined .....	1,603	
Patients infected .....	1,066	66.5
Infections:		
<i>Trichuris</i> .....	669	41.11
<i>Hookworms</i> .....	502	31.31
<i>Ascaris</i> .....	446	27.82
<i>Monads</i> .....	264	17.70
<i>Amoeba</i> .....	17	1.31
<i>Strongyloides</i> .....	7	0.43
<i>Tenias</i> .....	6	0.37
<i>Oxyuris</i> .....	3	0.17
<i>Hymenolepis nana</i> .....	1	0.06
Total infections .....	1,945	121.32

These results are not to be taken as the exact percentages of intestinal infections. It is to be admitted that each percentage of intestinal infection found represents the minimum obtained, for although two or more cover-glass preparations were made, still some might have escaped diagnosis.

TABLE II.—Comparison of infections by the common intestinal parasites with other reports.

Year.	Authority.	Country.	Examina-tions.	Infections.	Individuals infected.
1898..	Dobson <sup>a</sup> .....	India .....	1,249	1,340	P. ot. 107.28
1900..	Fearnside <sup>a</sup> .....	do .....	878	921	104.90
1901..	Colvert <sup>a</sup> .....	do .....	100	143	143
1904..	Anemia Commission <sup>a</sup> .....	Porto Rico.....	4,482	6,259	189.64
1908..	Garrison <sup>a</sup> .....	Philippine Islands, Bi-libid Prison.	4,106	7,636	8,447
1915..	P. H. S. <sup>b</sup> .....	do .....	13,297		87.7

<sup>a</sup> Garrison, *This Journal, Sec. B* (1908), 3, 194.

<sup>b</sup> Report of the Philippine Health Service for the year 1915 (1916), 16.

<sup>c</sup> Fecal specimens.

It will be seen from Table I that the number of infections is slightly greater than that found by Dobson or by Fearnside, but much less than that obtained by Garrison. The figures given by Colvert and by the Anemia Commission are not good for comparison, as the former examined only 100 persons, while the latter's work was for hookworm only and, consequently, not a true statistical statement of infections by intestinal parasites for the general population. The number of infected persons is about 70 per cent less than that obtained by Garrison, but almost equal to that reported by the Philippine Health Service in its annual report for 1915. The Filipinos examined by Garrison in Bilibid Prison in 1908 came from different parts of the Islands, and the Philippine Health Service report was for prisoners examined in 1915. Patients of the Southern Islands Hospital (1913–1916) came from the Visayan Islands—mostly from Cebu Island. How can we account for the great difference in results? The report of Bilibid Prison Hospital for 1915 shows 66.68 per cent, or about 1 per cent more than my findings here for patients admitted from 1913 to 1916. For this reason these data may be taken as the true statistical intestinal infection of the Filipinos for the period 1913 to 1916. That the number of infections is less than that obtained by Garrison in 1908 may be due either to the improvement in general sanitary conditions or to the education of the people with regard to personal hygiene.

#### GEOGRAPHICAL DISTRIBUTION

Attempts were made to find the infections by localities. In this case the last residences mentioned by the patients were taken as their true residences. The number of infected persons in each locality and the infections by *Trichuris*, hookworms, and *Ascaris* alone are compared.

TABLE III.—*Infections of patients by the common intestinal parasites in the Southern Islands Hospital.*

Locality.	Individuals.		Infected with—					
	Examined.	Infected.	Trichuris.		Hookworms.		Ascaris.	
			P. ct.	P. ct.	P. ct.	P. ct.		
City of Cebu .....	728	477	65.52	326	44.77	187	22.68	223 30.63
Towns of Cebu Province.....	691	468	67.72	270	39.07	261	37.77	176 25.47
Cebu Province, including the city of Cebu.....	1,419	946	66.59	596	42.00	448	31.57	399 23.11
Outside of Cebu Island .....	184	121	65.78	78	39.67	54	29.54	47 25.54

Table II shows that the percentage of infected persons varies from 65 to 67 and that of *Trichuris* from 39 to 44. Hookworm and *Ascaris* infections vary greatly. In Cebu city, hookworm infection is 12 per cent less than in the towns of Cebu Province, while it is 5 per cent more than that of *Ascaris*. If we believe that the sanitary condition of the city of Cebu is better than that of other towns of Cebu Province, we can deduce that hookworm infection is greatly influenced and lessened by improvement of sanitation and *Ascaris* infection is altered only slightly, if at all. The individual infections of *Trichuris*, hookworm, and *Ascaris* in Cebu Province and outside of Cebu vary only from 2 to 3 per cent.

#### DISTRIBUTION BY SEX

Out of 1,603 patients examined, 354 were women. The following gives their corresponding infections.

TABLE IV.—*Infections of males and females by the common intestinal parasites.*

Sex.	Individuals.		Infected with—					
	Examined.	Infected.	Trichuris.		Hookworms.		Ascaris.	
			P. ct.	P. ct.	P. ct.	P. ct.		
Males .....	1,249	810	65.58	496	39.71	423	38.86	328 26.26
Females.....	354	247	69.77	178	48.87	79	22.31	118 33.61

The females showed about 4 per cent more infections than the males. Infections with *Trichuris* and *Ascaris* were more numerous in the females; infections with hookworm were more numerous in the males. A greater percentage of hookworm infection in men than in women is to be expected for the reason that

infection of hookworm takes place mostly through the skin, especially of the legs and feet, and as a consequence the men, whose work is mostly out-of-doors, are naturally more liable to infection than women.

#### DISTRIBUTION BY AGES

To obtain an idea of the distribution of infection by ages, I divided the persons examined into decades from the first to the sixth. The seventh decade and over are included in the sixth decade. Table V shows the result.

TABLE V.—*Infestation by ages by the common intestinal parasites.*

Decade.	Individuals.		Infected with—		
	Examined.	Infected.	Trichuris.	Hookworms.	Ascaris.
1st.....	98	63	64.28	43	44.08
2d.....	355	274	77.18	176	49.85
3d.....	615	393	68.79	242	39.12
4th.....	241	153	63.48	97	40.24
5th.....	164	89	60.36	55	33.53
6th and 7th.....	120	84	65.12	66	43.41

The greatest infection percentage is in the second decade, while the least is in the fifth. The variation is not great even in the case of *Trichuris*. In the case of hookworm and *Ascaris* differences are marked in the first and second decades. In the first decade hookworm infection is the lowest. In ascariasis the greatest percentage of infection in the first decade may be explained partly by the fact that children are fed by the mothers, who may be infected and whose personal hygiene is very limited. Unsanitary conditions of the house and surroundings may largely be contributing factors in the production of this greater percentage of ascariasis in the first decade. These facts might suggest that more instruction in taking care of children be given to the mothers.

#### SYMPTOMATOLOGY AND PATHOGENICITY

*Trichuriasis*.—The presence of *Trichuris trichiura* in the intestine has never been recognized in this hospital by any characteristic symptom that it may have produced, but only by finding the ova by microscopic examination of the stool. Although many consider that whipworm infection is of little importance, a review of the literature on this subject indicates that, if it is not patho-

genic in many cases, still it aids greatly in the aggravation of other diseases. That the whipworm is pathogenic in some cases has been illustrated in the report of Musgrave, Clegg, and Polk.<sup>1</sup>

Four detailed cases of trichocephaliasis were mentioned: two producing severe progressive secondary anaemias followed by death in one and no improvement in the other after one month of treatment; the third producing the symptoms of diarrhoea, muscular cramps, dizziness, oedema, and indigestion; and the fourth a variety of symptoms, which on autopsy showed no cause other than an embolism of the left coronary artery by an adult *Trichuris trichiura*. The above illustrations and the fact that *Trichuris trichiura* has been found in the appendix after operation at the Southern Islands Hospital, which confirms the statement in several textbooks<sup>2</sup> that it occasionally causes appendicitis and wounds which serve as entrance for microorganisms into the blood stream, indicates that more attention should be paid to whipworm infection than it receives at present.

*Ankylostomiasis*.—In the great majority of cases the presence of hookworm is demonstrated solely through the routine stool examination of every patient admitted to the hospital rather than because of any symptom of its presence. All the symptoms produced by hookworm infection as described in the textbook of Castellani and Chalmers are seldom observed in the Filipinos admitted to the Southern Islands Hospital. Anaemia was seldom present with hookworm infection among Filipino patients, and those who were anaemic were mostly so due to malarial cachexia, tuberculosis, or some other cause.

We have had several cases, however, which we diagnosed as true cases of ankylostomiasis. In these cases our diagnosis was based upon the history of eating nonedible materials, such as earth and coal, feeling of laziness of the patient, and the symptoms of secondary anaemia. On examination of the stools diagnosis in all these cases was confirmed.

*Ascariasis*.—The infection of *Ascaris* produces mostly no symptoms among Filipinos, and if it does, the symptoms are very variable and not characteristic. One symptom that may be suggested of *Ascaris* infection is a dull abdominal pain which may or may not be accompanied by fever. Few cases of this complaint were observed in this hospital that could not be attributed to causes other than that of infection by *Ascaris* and in which

<sup>1</sup> This Journal, Sec. B (1908), 3, 545.

<sup>2</sup> Castellani and Chalmers, Manual of Tropical Medicine, 2d ed. William Wood & Company, New York (1913), 1801.

treatment of *Ascaris* entirely relieved the pain. Fever simulating the beginning of typhoid has been observed in many cases with *Ascaris* infection, in which, after administration of santonin and calomel, the temperature returned to normal. Whether the fevers of three or six days, which disappeared after treatment of *Ascaris*, were due to *Ascaris* infection is hard to tell, but the fact is that after removing *Ascaris* in some of those cases the patients were cured. In children convulsions and fever were observed which, after administering appropriate treatment, ceased with the subsequent recovery of the patients. Secondary anaemias due to infection with *Ascaris* are also not uncommon.

In general, it may be said that Filipinos seem to be more or less immune to the effects of *Ascaris* and hookworm infections. Even in children I have observed 35 and 42 *Ascaris* worms expelled, in one of 5 years of age and the other of 3 years of age. Both of these children were well developed and well nourished without any symptoms of intestinal parasites. They were admitted to the hospital as cholera carriers, and infections of *Ascaris* and hookworm were discovered only upon routine stool examinations.

#### TREATMENT

The drugs that are advocated by many authors for *Ascaris* and hookworm infections are the ones that have been used in the routine treatment of ascariasis and ankylostomiasis. The following order has been given for hookworm treatment:

Nothing to eat; stop all medicine and give magnesium sulphate saturated solution, 40 cubic centimeters at once.

After three hours give thymol, grains XL, one dose. Followed in two hours by magnesium sulphate saturated solution, 40 cubic centimeters.

Liquids may be given after free purgation.

Following day give usual treatment diet.

The following order was instituted in the treatment of ascariasis:

Give at one dose the following:

Santonin	grains V
Calomel	grains II
Sodium bicarbonate	grains V

Follow in five hours with magnesium sulphate saturated solution, 40 cubic centimeters.

The above treatments serve their purpose, but they are not ideal, as shown by the fact that in most cases the treatments were repeated many times before a complete elimination of the worms

resulted, as shown by the negative microscopic findings of the stool.

To observe the effects of broken doses, the same drugs with the same amounts were given as follows:

Nothing to eat; stop all other medicine and give magnesium sulphate saturated solution, 40 cubic centimeters.

After two hours give thymol, grains XL, in four doses at half-hour intervals.

After the last dose, repeat magnesium sulphate saturated solution.

For *Ascaris* treatment the following was substituted:

Give the following formula in four broken doses, half hour apart:

Santonin	grains V
Calomel	grains II
Sodium bicarbonate	grains V

After three hours of last dose, give magnesium sulphate saturated solution, 40 cubic centimeters.

These broken doses were given for two months, and the effects were compared with those in which the drugs were given in one dose for two months also.

TABLE VI.—Comparison of effects of one dose and of broken doses.

ASCARIS.

Results of one dose.		Results of broken doses.	
Persons treated.	Treatments given to produce negative finding for ova.	Persons treated.	Treatments given to produce negative finding for ova.
4	2	6	2
2	3	2	3
1	6	1	4
1	7	1	7

HOOKWORMS.

3	1	11	1
3	2	1	2
2	4		

From the tabulation it will be seen that the results of the treatment of *Ascaris* did not vary greatly, whether the formula was given in one dose or in four broken doses. As to hookworm treatment, it seems from the observation of the 8 and 12 cases that the broken doses are more effective in eliminating the hookworms than when giving the thymol in one dose.

**SUMMARY AND CONCLUSIONS**

The total intestinal infections among the Filipinos in the Visayan Islands examined in the Southern Islands Hospital is 121 per cent.

The percentage of infected individuals is 66.5.

The *Trichuris* infection alone is 41 per cent.

The hookworm infection alone is 31 per cent.

The *Ascaris* infection alone is 27 per cent.

*Ascaris* infection is greater in the city of Cebu than in the towns of Cebu Province, while the reverse is true with hookworm infection.

The second decade has the greatest percentage of infection.

The symptoms of intestinal infections among Filipinos are indefinite, and it seems apparent that the Filipinos are not very susceptible to intoxication of hookworm as compared with the white race.

The treatment of *Ascaris* infection with santonin and calomel, though it serves the purpose of eliminating the worms after several treatments, is not ideal.

The treatment of hookworm infection is more effective when the thymol is given in broken doses than when given in a single dose.

## A CASE OF ADVANCED PREGNANCY IN THE BROAD LIGAMENT<sup>1</sup>

By POTENCIANO GUAZON

(From the Department of Surgery, College of Medicine and Surgery, and the Philippine General Hospital, Manila)

F. G., 38 years old, Filipina, housewife, born and residing in Manila, was admitted to the surgical service of the Philippine General Hospital complaining of enlargement of the abdomen. Her father and mother died of diseases unknown to the patient. Her husband is living and well. The patient denies having had venereal diseases. There was no history of tuberculosis or tumor.

She had smallpox in childhood. Has occasional headache and fevers of short duration. Other diseases are denied.

Menses began at the age of 17 years. They have been regular, of about three days' duration, without any accompanying symptom till the sixth pregnancy, when she aborted, and afterward her menstruation became scanty in amount, lasting only for one or two days and always accompanied by pain transmitted to the upper region of the abdomen. She denies having any vaginal discharge.

The patient has had eleven normal deliveries. No history of puerperal infection was elicited. As stated above, she aborted her sixth pregnancy at the third month. At this abortion she had continuous bleeding for two weeks, which was at first profuse and gradually decreased in amount until it disappeared spontaneously. Her last delivery took place five years ago, being at full term and perfectly normal. Every time she became pregnant she had severe morning sickness lasting for two or three months. During this time she usually became nauseated and could not eat anything except sour food.

Five months ago she felt paroxysmal pain in the lower abdomen, usually at night. Later she noticed a tumor mass growing in the same region, which gradually increased in size and was slightly painful at times. During these months her menses stopped entirely, but she did not notice any other symptoms of

<sup>1</sup> Read before the Manila Medical Society, April 3, 1916.

pregnancy, except that she was becoming fleshy and her breasts were slightly enlarged, though painless and not containing milk. Her appetite has been usually good. The bowel movements are regular.

#### PHYSICAL EXAMINATION

The patient is well developed and nourished and is able to be about without discomfort. The sensorium is clear. Examination of the body reveals nothing important except the following:

Chest. The breasts appear slightly enlarged, but no secretion could be obtained from them, even on strong pressure. No other signs of importance.

Abdomen. There is a bulging occupying almost the whole lower part, reaching to midway between the umbilicus and symphysis pubis. It appears globular and free from the anterior abdominal wall. It is movable and can be pushed in all directions. There is slight fluctuation; the sensation is much like that of a fluid under high tension. The mass measures about 20 by 20 centimeters and is not tender on pressure. The greatest circumference of the abdomen passing over this tumor is 93 centimeters.

Vaginal examination. The perineum is lacerated in the second degree. The vaginal mucosa is of normal color. The cervix is soft, slightly edematous, and follows with the mass described above, when moved. The body of the uterus cannot be felt due to the pressure of the tumor.

As the history given by the patient is somewhat misleading, the diagnosis of ovarian cyst or some kind of tumor was suspected by the resident surgeon in charge of the case before operation.

#### OPERATION

The patient was operated upon by me. A low median incision was made. On opening the peritoneum, a tumor mass was encountered filling the lower abdomen, rather toward the left iliac region. Its surface is covered with numerous dilated vessels. It was of uneven consistence, soft in some parts and firm in other places. A cannula was introduced, but pure dark blood only was obtained. On manipulation, a piece of cauliflowerlike tissue came out and a suspicion of papilloma was then entertained; but while shelling off the tumor from the folds of the left broad ligament, a hairy surface appeared. Then the mass was opened, and a foetus of about five months was found.

The foetus was between the folds of the broad ligament displacing the uterus, which was enlarged and soft, toward the right side. The placenta was shelled out entirely by the fingers.

The bleeding, which was considerable, was stopped partly by pressure and partly by means of ligatures. The raw surface of the uterus was covered up, and the abdomen was closed without drain.

The patient had no postoperative complications and was discharged in good condition two weeks after the operation.

#### PATHOLOGIC EXAMINATION OF THE PLACENTA AND OTHER TISSUES REMOVED WITH IT

A careful examination of the specimen showed that a portion of the placenta was firmly attached to the fallopian tube and ovary. The case can be interpreted, therefore, as one of tubo-ovarian pregnancy at the beginning, which became intraligamentous later, following a rupture into the folds of the broad ligament.

#### DISCUSSION

The case related here and other similar cases of ectopic pregnancy are generally admitted as relatively uncommon gynecological affections. Because of their infrequency and lack of definite pathognomonic symptoms, they are not easily diagnosed and are very often mistaken for other pathologic conditions.

If it is true that, in the reported case, menstruation had been absent for about five months, the same condition may also occur, however, in an ovarian cyst, although such is not the rule. Besides, the patient is almost at the period of menopause, being 38 years of age.

The enlargement of the breasts alone, without the presence of other signs accompanying an ordinary pregnancy, may take place also in certain genital tumors.

The oedematous appearance of the cervix might have been caused, just as well, by pressure from the tumor mass, which displaced the uterus to one side. This same pressure and displacement producing passive congestion may also cause enlargement of the uterus.

Auscultation was not employed in the case, but as the fœtus was delivered apparently dead, its result would have been probably negative.

However, in diagnosing a case of ectopic gestation, we must take into account that the symptoms and signs usually found in an ordinary pregnancy are frequently obscure or wanting in the former affection, and for this reason it is advisable not to neglect any findings that may be obtained from history or from physical or laboratory examination which may point to the suspicion of such a condition.

In the reported case, for instance, such findings as cessation of menstruation corresponding to the period of growth of the abdominal swelling, fullness of the breasts, soft, edematous cervix, and a period of sterility for five years may be taken as sufficient data to arouse suspicion of the disease. But as this affection is not as common as tumors of the ovary and uterus, such as ovarian cysts, fibroids, etc., the exact condition is not as a rule diagnosed.

I recall that in the surgical service of Doctor Davis, in the Philippine General Hospital about three years ago, there was a case of advanced extra-uterine pregnancy which was diagnosed as tumor before operation. Nearly two years ago Roxas<sup>(6)</sup> reported to the Colegio Medico-Farmaceutico two cases of abdominal pregnancy (secondary) at full term, from the obstetrical service of Doctor Calderon in the same hospital. One of them was not diagnosed as such, but, apparently, as a case of intra-uterine pregnancy. It is to be observed that both patients came to the hospital calling for delivery.

The proportion of extra-uterine to intra-uterine pregnancies cannot be exactly determined, as statistics vary according to individual reports and those coming from the different clinics. According to Hirst,<sup>(2)</sup> it is given by some writers as being 1 to 500 approximately. From 1908 to 1915, in our surgical service, we had about 40 cases of ectopic pregnancy which, compared with the 5,000 cases of delivery registered in the obstetrical department of the College of Medicine and Surgery, during the same period, will show a proportion higher than that mentioned above.

The majority of the cases of ectopic gestation do not reach an advanced stage,<sup>(1)</sup> as they become ruptured or aborted during the early months of their development, resulting in the destruction of the fertilized ovum. Taking, for example, tubal pregnancies, which are the commonest types of ectopic gestation, according to Winkle<sup>(3)</sup> about 6 per cent of them only may proceed to full term. Hirst<sup>(4)</sup> reported two cases of tubal pregnancy that ruptured in two weeks. In our series of 65 cases, 2 progressed to full term (Calderon and Roxas), and there are 2 others that reached only the age of four to five months (Davis and Guazon).

In regard to treatment of advanced ectopic pregnancy, some gynecologists advise not to interfere until full term or until the stage of viability has been attained; while others do not distinguish any condition and operate as soon as the diagnosis is suspected or established. I see no objection to an early inter-

vention, if we consider that this kind of gestation is an abnormality and consequently may endanger the life of the patient at any time. We know also from statistics that a great number of foetuses or babies delivered from extra-uterine pregnancies are found either dead or deformed or live only for a short time.(5) In our case, like Dr. Davis's, the foetus appeared deformed and was delivered without signs of life. One of Doctors Calderon and Roxas's cases was also deformed and survived only for about ten minutes.

As to the management of the placenta, there is again a difference of opinion, as there are operators that favor its removal in one or more sittings. If the placenta can be removed without causing a fatal hemorrhage or other serious complications, it should be always done, in order to shorten the convalescence of the patient. The technic of operation will depend much on the anatomical findings on exploration, so that the procedure will vary according to individual cases. In our particular case the sac and placenta were taken out completely, and the abdominal incision was closed without drain.

#### REFERENCES

- (1) GUAZON, P. *Rev. Filipina Med. y Farm.* (1913), 4, 187.
- (2) (3) (4) HIRST'S Text-Book of Diseases of Women. W. B. Saunders Co., Philadelphia (1905).
- (5) HORSLEY, J. *Surg., Gyn. & Obst.* (1913), 1, 58.
- (6) ROXAS, B. *Rev. Filipina Med. y Farm.* (1915), 6, 687.



## ANNOUNCEMENT

Following an arrangement entered into between the Manila Medical Society and the Philippine Journal of Science, beginning with the year 1917, the latter will publish the minutes and abstracts of the proceedings of the meetings of the Manila Medical Society as evenly distributed as possible throughout the six issues of Section B, Tropical Medicine, of the Philippine Journal of Science. The Manila Medical Society submits its own copy. The arrangement is undertaken for the calendar year 1917 and succeeding calendar years until terminated in writing at the close of any year by either party. All original papers or articles read before the Manila Medical Society and bearing on the science of tropical medicine as shall be deemed by the Manila Medical Society to be worthy of publication in their entirety will be accepted for publication in Section B, Tropical Medicine, of the Philippine Journal of Science, as heretofore, under the same conditions as apply to articles submitted for publication from other sources. When an article is to be published in full in the Philippine Journal of Science, it will be referred to only very briefly or by title in the minutes and abstracts of the proceedings of the meetings of the Manila Medical Society. The pages of the minutes and abstracts of the proceedings are to be separately numbered and at the end of each year indexed in accordance with copy furnished by the society.

ALVIN J. COX,  
*General Editor,*  
*Philippine Journal of Science.*



## PROCEEDINGS OF THE MANILA MEDICAL SOCIETY

ANNUAL MEETING, JANUARY 6, 1917

On the evening of January 6, 1917, the Manila Medical Society embarked for the annual business meeting on the U. S. Army transport *Merritt* for Corregidor as the guests of the officers of the Medical Corps stationed on the island.

The following report of the proceedings of the meeting of the Manila Medical Society is taken from the minutes of the secretary, Lieut. H. G. Maul:

The regular monthly and annual meeting of the Manila Medical Society was held at Corregidor in the hospital building on the evening of January 6, 1917.

The meeting was called to order by the president, Dr. B. C. Crowell, who immediately appointed Dr. John A. Johnston, Dr. R. B. Gibson, and Capt. J. H. Trinder as a committee on nominations for the officers of the society for the ensuing year.

The minutes of the previous meeting were read by Dr. C. H. Manlove and were approved as read. Doctor Crowell then stated that arrangements were about to be completed in which the annual dues for membership would also entitle the members to Section B of the Philippine Journal of Science.

The nomination committee then returned and recommended for president, Lieut. Col. F. A. Winter, M. C., U. S. Army; for vice president, Dr. E. S. Ruth; for secretary and treasurer, Lieut. H. G. Maul, M. C., U. S. Army. There were no objections to the nominations, and it was moved and seconded to accept the recommendations of the committee. Prof. F. G. Haughwout then made a motion that the secretary be instructed to cast a unanimous ballot in favor of these nominations. It was seconded by Doctor Johnston. The new officers were then formally installed.

There then followed an informal scientific and social session and smoker. Dr. Paul Clements spoke of the work and the problems of the Philippine Health Service. Dr. N. M. Saleeby discussed the duties of the civilian practitioners and their relation to the military and naval medical corps. Major Rutherford gave an account of the case of anterior poliomyelitis lately discovered at Corregidor and enumerated in detail the quarantine measures that had been taken.<sup>1</sup> Other speakers in lighter vein

<sup>1</sup> See minutes of the subsequent meeting, February 13, 1917.

were Lieut. Col. J. T. Clarke; Col. C. L. Philipps, C. A. C.; Maj. W. M. Fassett, 13th Infantry; Lieut. Col. A. W. Kimble, Q. M. C.; Capt. Alex. Hall; and Capt. Franc Lecocq, C. A. C.

Professor Haughwout then moved that a vote of thanks be extended to the Quartermaster Corps, Colonel Crosby, Major Manly, Captain Trinder, the medical officers of Corregidor, and the program committee. The motion was seconded by Doctor Crowell. It was unanimously carried.

Doctor Gibson then moved that a vote of thanks be extended to the outgoing officers of the society. This motion was seconded by Doctor Johnston and was unanimously carried.

En route a business meeting of the Philippine Islands Medical Association was held, a report of which is as follows:

#### MINUTES OF THE PHILIPPINE ISLANDS MEDICAL ASSOCIATION

MEETING HELD JANUARY 6, 1917

In the absence of the president and both vice presidents, the meeting was called to order by the secretary-treasurer. On motion, seconded and carried, Councillor Saleeby was directed to take the chair.

The secretary-treasurer announced that the business of the meeting was the election of officers. On motion, duly seconded and carried, the association proceeded to the election of officers.

The nominating committee appointed by the chair presented the following names:

For President:	Dr. B. C. Crowell.
For First Vice President:	Dr. A. G. Sison.
For Second Vice President:	Dr. Thos. F. Keating.
For Councillor for five years:	Dr. S. V. del Rosario.
For Councillor for four years:	Dr. José Albert.
For Councillor for two years:	Maj. Clarence J. Manly, U. S. Army.
For Councillor for one year:	Capt. Charles C. Hillman, U. S. Army.

There being no further nominations, the secretary-treasurer was instructed to cast a unanimous ballot for the association for each of the above officers.

Doctor Crowell took the chair.

On motion to adjourn, duly seconded and carried, the meeting was adjourned at 8.20.

R. B. GIBSON,  
*Editor of the Proceedings,*  
*Manila Medical Society.*

THE PHILIPPINE  
JOURNAL OF SCIENCE  
B. TROPICAL MEDICINE

VOL. XII

MARCH, 1917

No. 2

EXPERIMENTAL CHOLERA CARRIERS AND IMMUNITY<sup>1</sup>

By OTTO SCHÖBL and C. S. PANGANIBAN

(From the Biological Laboratory, Bureau of Science, Manila, and  
the Quarantine Laboratory, Health Officer's Department,  
Port of New York)

In order to gain some information with regard to the relation between immunity and the state of cholera carriers in experimental animals, it was necessary to establish first of all the presence or the absence of immune bodies in the blood of experimental cholera carriers, then the presence or the absence of immune bodies in the bile of immunized animals, and finally to study the influence of artificially produced immunity upon the existence and the duration of the state of cholera carriers in experimental animals.

It has been stated in one of the previous publications<sup>(1)</sup> that immunity has been found to exist as a result of intravesicular inoculation. This question was studied extensively with regard to various microbes by Viole.<sup>(2)</sup> This author found that the serum of rabbits infected by intravesicular injection of various microbes contained immune bodies in the blood and that the content of the infected gall bladder conveyed specific immunity to normal animals. The immunity as produced by intravesicular injection of bacteria is so closely related to the study of cholera carriers that it was deemed advisable to arrange some experiments in that direction.

<sup>1</sup> Received for publication December 13, 1916.

**1. EXAMINATION OF THE SERUM OF EXPERIMENTAL CHOLERA CARRIERS FOR PRESENCE OF IMMUNE BODIES (AGGLUTININS)**

Guinea pigs and rabbits were infected by intravesicular injection in the usual way.(3) The guinea pigs were bled from the carotid artery; the rabbits, from the ear vein. The same strain of cholera vibrio that was used to infect the animals was also employed in performing the agglutination test. The results of these tests are tabulated as follows:

**TABLE I.—Showing the presence of immune bodies in the serum of experimental cholera carriers (guinea pigs). Agglutination test.**

[++, strong agglutination; +, weak agglutination; + tr., trace of agglutination; -, no agglutination.]

**CARRIER GUINEA PIGS.**

Guinea pig.	Days after inoculation.	Dilutions of serum.					
		1/10	1/20	1/40	1/80	1/160	1/320
1	7	+	+	+	+	-	-
2	7	+	+	+	+	-	-
3	7	+	+	+	+	-	-
4	8	+	+	+	+	+	-
5	10	+	+	+	+	+	-
6	10	+	+	+	+	+	-
7	11	+	+	+	+	+	-
8	11	+	+	+	+	+	-
9	11	+	+	+	+	+	-
10	11	+	+	+	+	+	+ tr.
11	16	+	+	+	+	+	-
12	16	+	+	+	+	+	-

**NORMAL GUINEA PIGS.**

1		+	+	+ tr.	-	-	-
2		+	+	+ tr.	-	-	-
3		+	+	+ tr.	-	-	-
4		+	+	+ tr.	-	-	-
5		+	+	+ tr.	-	-	-
6		+	+	+ tr.	-	-	-

It is evident from Tables I and II that both guinea pigs and rabbits, the latter to a higher degree than the former, show the presence of immune bodies in the blood as a result of intravesicular inoculation with cholera vibrios.

TABLE II.—*Showing the presence of immune bodies in the serum of experimental cholera carriers (rabbits). Agglutination test.*

[++, strong agglutination; +, weak agglutination; + tr., trace of agglutination; -, no agglutination.]

CARRIER RABBITS.

Rabbit.	Days after inoculation.	Dilutions of serum.							
		1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280
1.	0	+	-	-	-	-	-	-	-
	5.	++	++	++	++	+	-	-	-
2.	0	+	-	-	-	-	-	-	-
	6	++	++	++	++	++	++	+	-
3.	0	+	-	-	-	-	-	-	-
	7.	++	++	++	++	++	+	-	-
4.	0	+	-	-	-	-	-	-	-
	10.	++	++	++	++	++	++	+	+
5.	0	+	-	-	-	-	-	-	-
	6.	++	++	++	++	++	++	+	-
6.	12.	++	++	++	++	++	++	+	-
	17.	++	++	++	++	++	++	+	-
7.	22.	++	++	++	++	++	++	+	-
	28.	++	++	++	++	++	++	+	-
8.	38.	++	++	++	+	-	-	-	-
	49.	++	++	++	-	-	-	-	-
9.	57.	++	-	-	-	-	-	-	-

The following experiment is included merely for the sake of completeness:

One rabbit was immunized by intravenous injections of  $\frac{1}{10}$ ,  $\frac{1}{6}$ ,  $\frac{1}{2}$ , and 1 slant of heated cholera culture. Twelve days after the last injection a sample of blood was withdrawn from the rabbit's ear vein and about 0.5 cubic centimeter of bile was aspirated from the animal's gall bladder by means of a syringe. Both the blood and the bile, which latter was of normal color and appearance, were subjected to agglutination tests in dilutions of from  $\frac{1}{10}$  to  $\frac{1}{1280}$ . The serum of this rabbit agglutinated cholera vibrios promptly in all dilutions. No agglutination was noticed in the test tubes containing dilutions of the bile.

One rabbit was immunized by intravenous injections of  $\frac{1}{10}$ ,  $\frac{1}{6}$ ,  $\frac{1}{2}$ , and 1 slant of heated cholera culture. On the twelfth day after the last injection this animal was infected with  $\frac{1}{10}$  of a slant of live cholera culture by intravesicular injection. Twenty-four hours after the infection the bile was withdrawn from the

gall bladder by means of a syringe. A sample of blood was also taken from the ear vein. The bile was of a light yellowish color and contained a large amount of mucus. No blood was found upon microscopical examination of the contents of the gall bladder. Centrifuged, it became clear and was subjected to the agglutination test. The serum showed positive agglutination in all dilutions up to  $\frac{1}{1200}$ . The contents of the gall bladder gave positive agglutination in dilutions  $\frac{1}{10}$  and  $\frac{1}{20}$ . Since the results of this experiment as well as those of the preceding tests are in accord with the results arrived at by Viole in his studies on this particular question, it was thought unnecessary to extend our experiments any further. The most important facts bearing on the question of experimental cholera carriers, namely, the presence of immune bodies in the blood of experimental cholera carriers and their occurrence in the content of infected gall bladder in immunized animals, has been demonstrated. Considering the findings of Viole and our own, one is inclined to expect that vaccination should exert some influence upon the state of cholera carriers in experimental animals.

In order to decide this important question, the following experiments were arranged:

## II. PREVENTIVE VACCINATION AND EXPERIMENTAL CHOLERA CARRIERS

A series of guinea pigs was immunized by injecting a suspension of cholera vibrios in physiological salt solution heated at 60° C. for thirty minutes. These injections were given either under the skin or intraperitoneally. At intervals of time, given in Table III, the vaccinated animals were infected with live cholera culture by intravesicular injection. One tenth of a slant of live cholera culture was injected. A series of normal animals, that is to say guinea pigs that had received no preventive treatment, was infected simultaneously and in the same manner as the immunized ones. At intervals varying from one to thirteen days after the intravesicular infection the animals were killed and the various sections of the digestive system were examined for the presence of cholera vibrios. The thirteenth day was taken as the upper limit of time, since it became known in previous experiments<sup>(3)</sup> that after the fourteenth day some of the experimental carriers became spontaneously negative.

TABLE III.—*Showing the number of takes and the duration of the state of cholera carriers in immunized and nonimmunized animals.*

[+, cholera vibrios found; —, cholera vibrios not found; vn, very numerous, more than 200 colonies; n, numerous, about 200 colonies; f, few, about 12 colonies; vf, very few, less than 6 colonies.]

Guinea pig.	Immunized.		Infected, days after vaccine.	Killed, days after infection.	Direct plates.			Peptone cultures.		
	Dose in slants.	Mode of immunization.			Bile.	Duodenum.	Ileum.	Cæcum.	Gall bladder.	Duodenum.
1	1/10, 1/5, 1/2, ...	Subcutaneously.	8	1	o	o	o	o	+	+
2	1/10, 1/5, 1/2, 1, ...	do	8	5	n	f	f	-	+	+
3	1/10, 1/5, 1/2, 1, ...	do	8	5	f	-	-	-	+	+
4	1/100, 1/20, 1/2, 1, ...	Intraperitoneally.	8	5	n	n	f	-	+	+
5	1/10, ...	Subcutaneously.	19	6	f	vf	f	-	+	+
6	1/10, 1/5, ...	do	19	6	n	f	n	-	+	+
7	1/10, 1, 1/5, 1/2, ...	do	19	6	n	f	-	-	+	+
8	1/100, ...	Intraperitoneally.	10	7	n	f	f	-	+	+
9	1/100, 1/50, ...	do	10	7	n	n	n	-	+	+
10	1/100, 1/50, 1/20, ...	do	10	7	n	n	n	-	+	+
11	1/10, 1/5, 1/2, 1, ...	Subcutaneously.	10	9	vf	-	vf	-	+	+
12	1/10, 1/5, 1/2, 1, ...	do	10	10	vf	-	vf	-	+	+
13	1/10, 1/5, 1/2, 1, ...	do	10	13	-	-	-	-	+	+
14	1/10, 1/5, 1/2, 1, ...	do	10	14	vn	-	n	-	+	+
15	1/10, 1/5, 1/2, 1, ...	do	10	14	-	-	-	-	+	+
16	1/10, 1/5, 1/2, 1, ...	do	10	14	f	vf	-	-	+	+

#### NONIMMUNIZED CONTROLS.

17					5	f	-	f	vf	+
18					5	n	f	n	vf	+
19					7	n	f	f	vf	+
20					9	vf	-	vf	vf	+
21					10	vf	-	vf	vf	+
22					13	vf	-	vf	vf	+
23					14	n	vf	-	-	+
24					14	n	-	-	-	+
25					14	-	-	-	-	+

### III. VACCINE THERAPY OF EXPERIMENTAL CHOLERA CARRIERS

A series of guinea pigs was infected by intravesicular injection. After the infection some of these animals were vaccinated by subcutaneous injection of heated cholera cultures. From seven to thirteen days after the infection they were killed and examined. The thirteenth day was taken as the upper limit for the reason already given.

TABLE IV.—*Showing the duration of the state of cholera carriers in treated and in untreated animals.*

[+, cholera vibrios found; —, cholera vibrios not found; vn, very numerous, more than 200 colonies; n, numerous, about 200 colonies; f, few, about 12 colonies; vf, very few, less than 6 colonies.]

Guinea pig.	Days after infection.	Treatment.	Mode of immunization.	Killed after infection.		Direct plates.				Peptone cultures.			
				Days after last vaccine.	Bile.	Duodenum.	Ileum.	Cæcum.	Gall bladder.	Duodenum.	Ileum.	Cæcum.	
1	1	1/10.....	Subcutaneous.	7	vn	—	n	—	+	+	+	—	—
2	1	1/10.....	do	3	vn	n	vn	—	+	+	+	+	—
3	6	1/10.....	do	7	1	vn	vn	vn	+	+	+	+	—
4	1	1/10, 1/5, 1/2	do	9	6	f	vf	—	+	+	+	+	—
5	1	1/10, 1/5, 1/2	do	9	3	n	n	n	+	+	+	+	—
6	4	1/10, 1/5.....	do	10	4	vf	—	—	+	+	+	+	—
7	4	1/10, 1/5.....	do	11	4	n	—	vf	+	+	+	+	—
8	4	1/10, 1/5.....	do	11	4	f	—	vf	+	+	+	+	—
9	1	1/10, 1/5.....	do	12	vn	vn	—	—	+	+	+	+	—

#### UNTREATED ANIMALS.

10	.....	.....	.....	9	n	vf	f	—	—	+	+	+	+
11	.....	.....	.....	10	vn	n	f	—	—	+	+	+	—
12	.....	.....	.....	11	n	—	vf	—	—	+	+	+	—
13	.....	.....	.....	11	vn	f	n	f	—	+	+	+	—
14	.....	.....	.....	12	vn	n	n	—	—	+	+	+	—

These tables show the results of experiments concerning the influence of immunization upon the state of experimental cholera carriers. Unless we interpret as an effect of immunization the one negative animal (guinea pig 13, Table III) and the apparent decrease of cholera vibrios in the intestinal canal, as indicated by absence of cholera colonies on direct plates, we fail to see any effect of immunization upon the cholera carrier state in experimental animals.

It must be admitted that the test is rather severe, because the mode of infection, namely, the introduction of a considerable amount of cholera culture directly into the gall bladder, gives the vibrios the best possible chance to gain a foothold in the gall passages. Again the short time of observation, limited to thirteen days after infection, hardly allows the immunity to develop the maximum of its action.

#### CONCLUSIONS

1. Specific immune bodies were found to be present in the blood serum of experimental cholera carriers (guinea pigs, rabbits).
2. Specific immune bodies were found to be absent in the normal bile of a highly immunized rabbit. In confirmation of Viole's findings specific antibodies were found to be present in the gall bladder contents of infected rabbits.
3. The percentage of takes in guinea pigs that received preventive inoculation or vaccine treatment was as high as in untreated carriers.
4. Preventive vaccination and vaccine therapy effected no apparent shortening of the duration of cholera carriers in guinea pigs.

#### REFERENCES

- (1) *Journ. Inf. Dis.* (1916), **19**, 145.
- (2) *Ann. Inst. Pasteur* (1912), **26**, 147, 381.
- (3) *Journ. Inf. Dis.* (1916), **18**, 307-314.



# STUDY OF THE ANATOMICOPATHOLOGIC LESIONS IN ONE THOUSAND FILIPINO CHILDREN UNDER FIVE YEARS OF AGE<sup>1</sup>

By MARIA PAZ MENDOZA-GUAZON

(From the Department of Pathology and Bacteriology, College of Medicine and Surgery, University of the Philippines)

The purpose of this work is to tabulate the anatomicopathologic lesions of Filipino children under 5 years as found at autopsy, for the purpose of comparison with the published results of workers in other countries and to find the influence of age and season on certain diseases. The majority of the cases came from the Philippine General Hospital, some from San Lazaro Hospital for communicable diseases, and a few from other sources.

This record does not indicate the causes of infant mortality in the city of Manila, yet it reflects them to a certain degree.

The autopsies have been performed by the different members of the pathological staff of the College of Medicine and Surgery, University of the Philippines, and comprise those performed from January, 1910, to March, 1916, a total of 1,000 cases, in a period of a little over five years.

## STILLBIRTHS

Of 52 cases of stillbirth, 5 gave unsatisfactory results from the standpoint of causation, owing in part to the unsatisfactory examination and in part to the insufficient knowledge of the maternal condition. Fifteen were premature and 5 were macerated foetuses. Of the remaining 32, in which anatomical investigation showed definite lesions which could account for the stillbirth, the causes can be classified as follows:

Asphyxia in utero, 4 cases; knot in the cord, 1; fracture of the skull, 4; multiple congenital anomalies, 2; cerebral hemorrhage, 2; intraperitoneal cyst with calcareous deposits and chronic adhesive peritonitis, 1; cephalohematoma, 10; rupture of the anterior intervertebral ligament, 3; hemorrhage into the adrenals (forceps case), subdural hemorrhage and atelectasis of the lungs and hyperplasia of the thymus gland, which weighed 87

<sup>1</sup> Thesis presented for the degree of Doctor of Tropical Medicine, 1916.  
Received for publication February, 1917.

grams, craniotomy, cleidotomy, ectopic gestation with peritoneal implantation of the placenta, and gelatinous mass in the abdomen (probably meconium), 1 each. Eight of the cases of cephalohematoma had meningeal hemorrhage, 2 subcapsular hemorrhage of the liver, and 1 hemorrhage in the adrenals and kidneys.

#### CAUSES OF DEATH FROM THE FIRST TO THE SIXTH DAY

Causes of death, first day, 19 cases. Hemorrhage, 12 cases; congenital atelectasis of the lungs, 4; volvulus of the intestine, artificial anus with bronchopneumonia, acute enteritis with hepatic cirrhosis, 1 each. Of the 12 cases of hemorrhage, 10 were in the cerebrum or meninges, 1 of these being caused by rupture of hernia cerebri frontalis, 2 were in the adrenals, 1 was in the duodenum. The last case was in a premature male of 7 months, who also had a hematoma in the inferior border of the left lobe of the liver; rupture of the liver; hemorrhage into the peritoneum, the thorax, and the adrenals; and slight atelectasis of the lungs.

Second day, 5 cases. Hemophilia neonatorum, multiple congenital anomalies, imperforate rectum, congenital umbilical hernia with the liver and part of the intestines inside an umbilical sac, and comminuted fracture of the temporal bones, 1 each. The last had also hemorrhage into the peritoneum, liver capsule, and adrenals probably following resuscitation.

Third day, 11 cases. Six of these were due to the following causes: Hemophilia neonatorum, atresia recti with pulmonary hemorrhage and scoliosis, icterus neonatorum with pulmonary atelectasis in a premature infant, internal hydrocephalus in a male twin, and secondary anæmia caused by hemorrhage from the umbilical cord, which was cut very short. Of the remaining 5, 3 had hemorrhage into the lungs and brain. Besides the hemorrhage into the lungs and brain, patent ductus arteriosus was found in 2 cases of the former and patent foramen ovale in 1 case of the former and in 1 of the latter.

Fourth day, 2 cases. One had hemorrhage into the right cerebellar hemisphere and the other hemorrhage into the lungs, internal hydrocephalus, and patent ductus arteriosus and foramen ovale. The last was a premature male, 7 months old.

Fifth day, 8 cases. Hemorrhage, 5 cases; suppurative meningitis, action of rats, and congenital syphilis, 1 each. Of the 5 cases of hemorrhage, 4 were subdural and accompanied by icterus, 1 of these had omphalitis, another streptococcæmia-

following an infected cephalohematoma, and another acute membranous enteritis, acute suppurative pancreatitis, acute choledochitis, and acute hemorrhagic nephritis. The case of suppurative meningitis had erosion of the skin covering a congenital sacral spina bifida (sacral meningomyelocele).<sup>(6)</sup>

Sixth day, 1 case. Hemorrhage in the lungs and acute gastro-duodenitis.

From this we can see that hemorrhage played a great part in causing death during the first days of life, but we cannot take this as the rule in the city of Manila, for many of our cases came from the obstetrical department of the Philippine General Hospital, whose mothers asked help only when all the outside resources were exhausted.

Knopfelmacher<sup>(29)</sup> says that hemorrhage in the newborn occurs frequently in unassisted as well as in assisted labors. The hemorrhage is in part traumatic in origin, in part, however, due to interruption in the placental circulation through compression of the cord or through asphyxia.

Holt<sup>(27)</sup> thinks that the predisposing cause of the frequency of hemorrhage in young infants is due to the extreme delicacy of the blood vessels and the great changes taking place in the blood itself and in the circulation as a result of the passage from intrauterine to extrauterine life. Without taking into consideration those cases due to trauma and those due to infection, he mentions a class in which the hemorrhages are not associated with any other known process and in which the bleeding is extensive, multiple in location, and spontaneous in origin, and ceases also in the same way.

Cautley<sup>(8)</sup> divides the hemorrhagic diseases of the newborn into three: accidental, traumatic, and pyogenic. He states that in true hemorrhagic disease there is a spontaneous capillary oozing, which begins at a variable period after birth and proves fatal or lasts for a few days to a few weeks and yet ends in recovery. The circulatory disturbances due to ligature of the cord at birth or compression of the cord during labor may cause hyperæmia of the mucous membranes and hemorrhagic oozing and extravasation throughout the body. Similar congestion can be produced by backward pressure from congenital heart lesions, the respiratory obstruction in asphyxia and atelectasis, and hepatic cirrhosis. Gastrointestinal hemorrhage may thus be a kind of epistaxis from the congested membrane in consequence of its sudden functional activity, possibly associated with deficient coagulability of the blood.

Schloss and Commiskey, (46) after investigating the coagulation of the blood in 10 cases of the so-called hemorrhagic disease of the newborn, came to the following conclusions:

1. In the hemorrhagic conditions of the newborn the coagulation of the blood may be normal, delayed, or absent.
2. A deficiency or absence of thrombin or fibrinogen may give rise to imperfect blood coagulation and uncontrollable hemorrhage.
3. In some cases of hemorrhage in the newborn in which blood coagulation is apparently normal, it seems probable that the hemorrhage is due to some localized vascular lesion or defect present only in the areas from which the bleeding occurs.
4. The subcutaneous injection of whole blood is harmless and is of apparent value in the treatment of hemorrhage.

Shaw and Williams (47) found the coagulation time in infants under 2 years shorter than in adults.

Tabulating our cases of hemorrhage as to place found in this series of 1,000 autopsies of children under 5 years, we have:

Hemophilia neonatorum, 2 cases.

Hemorrhage in the lungs, 9 cases. In one of these the hemorrhage of the lungs was associated with hemorrhage in the meninges and liver, one with atresia ani, one with acute gastrroduodenitis, and another had also intradural and basal hemorrhages of the brain.

Hemorrhage from the navel, 4 cases. Besides the hemorrhage, suppurative thrombophlebitis and bronchopneumonia were found in a 17-day-old infant.

Cerebellar hemorrhage, 6 cases. It is interesting to note the case of a premature infant that lived for fifty-one days with an old hemorrhage in the cerebellum and tuberculous mesenteric glands and that died of bronchopneumonia.

Subdural hemorrhage, 7 cases. In 5, atelectasis of the lungs was found; in 1, bronchopneumonia, icterus, and cirrhosis of the liver, and in the last, meningeal hemorrhage and omphalitis.

Brain and meningeal hemorrhages, 9 cases. One of these had also umbilical hemorrhage. In a baby 1 month old the hemorrhage became colligative, and in another 8 months old it was located in the left parietal region and was organized.

Meningeal hemorrhage, 16 cases. Atelectasis of the lungs was found in 9, and cephalohematoma was found in 4; both conditions were met in 3 cases. The hemorrhage was so extensive in a female 3 months old that the clinicians diagnosed it as eclampsia.

Fracture of the skull and hemorrhage, 9 cases. One of these had also hemorrhage in the liver.

**Retroretinal hemorrhage due to glioma, 2 cases.**

**Hemorrhage from the alimentary tract, 4 cases.** One was from a gastric ulcer in a male 25 days old that died of lobar and lobular pneumonia and acute nephritis; 1 a duodenal ulcer and complicated with suppurative otitis media; 1 from the urinary bladder and accompanied by ulcerative enterocolitis; and the last had also hemorrhage in the duodenum, hematoma in the left lobe of the liver, and cerebromeningeal hemorrhage. Hemorrhage in the adrenals is a frequent occurrence either alone or with hemorrhage of the other organs. Of the first we had 3 cases, and of the latter we had 4.

**Hemorrhage in the liver, 8 cases.** Of these, 4 were accompanied by hemorrhage of the brain or meninges; 2 of the adrenals; and of 2, of both organs.

**Rupture of the anterior intervertebral ligament at the level of the last cervical vertebra, 3 cases.** This is probably due to extreme anteflection of the head in performing Moriceau's maneuver for extraction of the head.

**ANOMALIES AND CONGENITAL DEFECTS****Heart and blood vessels, 21 cases.**

Patent foramen ovale, 19 cases; patent ductus arteriosus, 36; patent interventricular septum, 4; displaced heart to the right side, 1; and presence of two cusps in the pulmonary orifice, 1. The small number of cases with patent foramen ovale and ductus arteriosus is probably due to incomplete examination on the part of the pathologist.

**Brain.** There has been one case of each of the following: Porencephalus, hernia cerebri, meningocele, sacral spina bifida, long cerebellar peduncles, and microencephalia. The pseudotanics symptoms of the last have been reported by José Albert and M. P. Mendoza to the Philippine Medical Association (1912).

**Genitourinary system, 16 cases.** Horseshoe kidney, 2 cases; congenital cystic kidneys, 2; undescended testicles, 4; congenital hydrocele, 2; stricture of ureter, 1; left ureter coming from the lower anterior portion of the kidney, 1; cystic ovaries, 2; hernia of right tube and ovary in right inguinal canal, 1; bicornuate uterus, 1. One of the cases of undescended testicle had hernia in the right inguinal canal, and one of the cases of cystic ovaries was accompanied by patent interventricular septum. The infantile uterus has been found many times on the left side in my autopsies.

**Alimentary tract.** Tracheo-oesophageal anastomosis and multiple congenital anomalies, 1 case; imperforate rectum, 1; imperforate anus, 3; microcolon and omental adhesions, 1; gelatinous mass in abdomen, probably meconium, 1; congenital obliteration of the cystic duct with hydrops of the gall bladder, 1; congenital obliteration of the gall bladder, 1; cysts on either side of the oesophagus, 1; aberrant liver tissue in pancreas, 1; Meckel's diverticulum, 2; inguinal hernia, 2; congenital volvulus of the intestine 30 centimeters above the ileoæcal valve, 1. The last lived for one hour only, and at autopsy there was rupture of the ileum 2 centimeters below the twist. The 2 cases of hernia were found in males and in the right side.

**Liver.** Autopsy 3197 is a female infant that lived 39 hours. The liver and several loops of the small and large intestines were found inside a hernia of the umbilical cord. The small liver is entirely within the sac, except a small strip from the posterolateral edge of the left lobe that extends outward and downward to the anterior surface of the cardiac end of the stomach. The lower part of the Spighelian lobe is relatively enlarged and is directly in relation to the posterior surface of the lesser omentum.

**Lungs.** Left lung with three lobes, 2 cases; incomplete lobulation of the lungs, 1; malformation and misplaced right lung, which was found as a small mass beneath the left, 1; right lung with two lobes, 2.

**Bones.** Anomaly of fourth costal cartilage, 1 case.

**Spleen.** Accessory, 5 cases only are recorded.

**Ectopic gestation** with peritoneal implantation of the placenta, 1 case.

#### MULTIPLE CONGENITAL ANOMALIES

**Autopsy 2111.**—The mouth is very narrow, almost circular, and the buccal cavity just admits a leadpencil; the fourth and fifth fingers on each hand are fused; the inferior mandible is very pointed; the fourth and fifth toes are fused, and there is no uvula. Larynx is imperfectly developed, with cleft epiglottis and no vocal cords. Left kidney is cystic, right kidney and ureter missing. Lobes of liver symmetrical, and its median line is that of the abdomen. External genitalia are imperfectly developed, there being a small perforate organ which may represent penis or clitoris.

**Autopsy 1932.**—Male infant, born by breech presentation, with placenta attached by a short fibrous cephalic cord 1 centimeter in length, containing blood vessels which on dissection are con-

tinuous with the umbilical cord to a frontal meningocele. The fibers of the cephalic cord are continuous with the foetal membranes and with the covering skin of the meningocele.

The head is incomplete; there is no forehead above the superciliary ridges, but immediately above the left inner canthus and left inner side of the nose is a semiglobular mass about 2 centimeters in diameter, yellowish and dry, which during life contained cerebrospinal fluid and brain substance. From the forehead extends upward and around the head just about the level of the tops of the ears a large, thin cystic mass. The hair below this is well developed. The nose and mouth are much deformed. The right ala nasi is apparently formed, but is separated from the median portion of the nose by the nostril, which extends halfway to the bridge. There is an opening on the left side where the ala nasi is apparently deficient, orifices leading both into the left nostril and into a cavity between the left inner canthus and nose. The upper lip shows two divisions like the ordinary cleft palate in the superior portion, which makes the mouth large and the hard palate much deformed.

The three outer fingers on the right hand are imperfectly developed and form a single mass with 3 fingernails; the three fingers cannot be differentiated. This mass is about half as long as the first finger. The first finger and thumb are well proportioned. On the left hand the same description applies to the outer two fingers.

On the left foot the first and second toes are missing, apparently no phalanges having developed; the other three are very short and rudimentary. The toes on the right foot are normally developed.

The eyes are perfectly developed, but the right has a smaller opening at the expense of the palpebral skin, so that it could not be voluntarily opened during life. The chest is well shaped, rounded, and wide, and is very large. This baby lived for nineteen days.

*Autopsy 2146.*—Male with malformation of hands, wrists, and left forearm, imperfect interventricular septum, and undescended right testicle. Only one bone could be palpated in the left forearm, and the carpal bones as individual bones appear to be absent. The left thumb was an outgrowth at the end of the first phalanx of the first finger on its inner and outer aspect and was loosely attached.

*Autopsy 2282.*—Male that lived for two days with the clinical diagnosis of absence of penis and imperforate anus. This case is

interesting, for the anomalies were found at the junction of the ectoderm and endoderm. The post-mortem description is as follows:

In the pubic area is a sac covered with skin resembling a scrotum. In the midlateral portion of this on the right side is a slitlike fold of the skin with the convexity upward, from which there exudes pale, turbid fluid on pressure of the sac. The cæcum is beneath the margin of the liver, and the appendix is lying on the anterior surface of it.

The œsophagus is of normal caliber and is lined by a pale mucosa, but it ends in a blind pouch at its mid portion. The cardiac end seems to be of normal caliber and appearance and passes directly into the lower end of the trachea between the primary bronchi. The mucosa of the bronchi is continued on to that of the trachea, on its anterior wall especially showing the longitudinal striations of the mucosa.

The stomach is small and empty. The opening of the œsophagus into the stomach is normal, but the pyloric end of the stomach forms a blind pouch, which does not communicate with the duodenum.

The right lung has only two lobes.

The ductus arteriosus is widely open, forming a canal about 0.5 centimeter in diameter. The foramen ovale is also patent.

The kidneys are fused into one, forming a horseshoe, the junction between them being placed at the lower poles and overlying the lumbar vertebra. There are two ureters.

The lower part of the abdomen is occupied by a large, hollow mass, which extends into the pelvis. This is attached to the urachus, and passing over it from the right to the left is a thick, but partially patent, hypogastric vessel. This sac has a thick wall, about 0.5 centimeter in thickness, and is lined by mucosa which is hemorrhagic in its upper portion and looks similar to that of the urinary bladder. Entering this sac are the ureters, which are laterally placed, and posteriorly and internally to the entrance of the right ureter at a point about the right margin of the promontory of the sacrum there enters the lower end of the dilated large intestine; this is very much constricted at its opening into this sac. From the lower portion of the sac, passing beneath the symphysis pubis, is a narrow canal which almost immediately bulges out to form a large sac, this sac being in the interior of the sac which was described as occupying the scrotal region. It is lined by smooth pale mucosa and a small circular orifice which just admits a small probe communicating with the slitlike opening, which was described on the right

lateral margin of the scrotal sac. The large sac and that which is called the scrotal sac are filled with brownish yellow globular masses of a rather firm consistence with some turbid fluid, both being present also in the dilated large intestine.

Finkelstone and Ellis<sup>(17)</sup> reported the case of a full-term child with œsophagotracheal fistula. The œsophagus ended in a blind pouch at the fifth tracheal ring from the bifurcation, and at the third tracheal ring from the bifurcation the distal end of the œsophagus opened into the trachea, causing a stricture at this site. Macroscopically they did not find any continuity of the œsophagus between the third and fifth ring, not even a fibrous cord. The stricture, they think, is due to an overgrowth of cells, either endodermal or ectodermal or a combination of the two at the junction of the œsophagotracheal fistula.

They cite two important theories about this, that of St. Clair Thomson and that of Locee. The first says that it is an arrest of development rather than a pathological process in the foetus, while the second explains it embryologically, that is, that the proximal and distal portions of the œsophagus have different sources of origin. The buccal cavity, pharynx, and upper extremity of the œsophagus develop from the ectoderm, and the intestinal tract, including the distal portion of the œsophagus and respiratory apparatus, develop from the entoderm. Fistulous communications between œsophagus and trachea are almost always situated at its bifurcation, and the membrane separating them closes last at this location.

*Autopsy 1577.*—In this case the urethra opens near the exterior into a common passage with the rectum.

*Autopsy 4062.*—This male premature infant lived for about fifteen minutes after delivery. The clinical diagnosis of this case is hydramnios, and at autopsy there was found in the right side of the abdomen partly extending into the left side and into the pelvis and to the liver a greenish, very soft gelatinous mass of about 500 grams in weight. Intermingled throughout this there are small spherical bodies of 0.5 centimeter in diameter; these have a pale capsule surrounding them and contain a greenish gelatinous material. Some of these whitish bodies are located beneath the peritoneum over the anterior surface of the left kidney, and over the entire abdominal viscera there is a thin, delicate structure. The liver and spleen are adherent to the diaphragm. Over the coils of the small intestine in the right half of the abdomen is a greenish membranous structure binding them together. A similar case was autopsied after this series.

Dr. B. C. Crowell, pathologist, College of Medicine and Surgery, University of the Philippines, thought that the cause was an antenatal rupture of the intestine with peritonitis.

*Autopsy 4170.*—This female full-term baby lived for one month and fifteen days and died with an undetermined diagnosis. The anatomical finding is interesting, for the development of the heart and vessels and the cloacal region seem to have been arrested at the fifth month of foetal life.

The anus is reddened and very small and measures about 0.5 centimeter in diameter. This has been operated for atresia ani. The labia majora are not distinct. There is a protrusion in the genital region about the clitoris which seems to be a fold inclosing two small leaflets that are apparently the labia minora. Between these is an opening for both the urethra and vagina. Foecal material comes both from the artificial anus and genital opening. The relation of the urinary bladder, uterus, and its appendages and the dilated upper part of the rectum is normal. The lower part of the rectum is constricted, and its anterior portion is continuous with the posterior surface of the uterus, so that there is a continuous and free passage from the lumen of the rectum to the vagina and into the uterine cavity, which has a mesial septum that divides it into two cavities, each one opening freely with the corresponding fallopian tube and into the rectovaginal opening.

The posterior wall of the urinary bladder is well separated from the uterus externally, but the wall between it and the vagina is represented by a fold covered by mucosa and directed toward the urethral opening or cloacal opening, so that a probe passing through the latter could be directed into the urinary bladder, cavity of the uterus, or into the rectum.

The artificial anus is about 3 centimeters in length and communicates with the left horn of the uterus. The descending colon is dilated and contains well-formed faeces. The musculature is not hypertrophied, and the lumen measures about 7 centimeters in diameter.

The cardiovascular anomaly. The heart is dark blue and is placed transversely. The apex is blunt, and the right ventricle is more dilated, thicker, and more rounded than the left. The right auricle is more dilated than the left and contains clots of blood. The left auricle is small, especially the appendiceal portion, and the mitral orifice is also small. The foramen ovale is patent. The upper part of the interventricular septum is missing, so that both cavities empty into one common thick-walled

vessel which is bent to the left, giving at the concave portion a branch that divides into two, which are apparently the pulmonary arteries. At the convexity other branches also arise. This common vessel has three semilunar cusps, and behind the left and anterior ones the coronary arteries arise. There is a cord-like transparent tissue that has a thick center and thin ends that is fastened about the middle of the attachment of the anterior and right cusps. The upper part of the interventricular septum is concave, and anteriorly the end is between the left and right cusp and posteriorly between the posterior and left, so that two cusps are in the right ventricle and one in the left. The left iliac artery has a larger caliber than the right.

The lungs resemble the spread wings of a bird due to anomalous indentations, for the left has three lobes.

A Meckel's diverticulum is found 50 centimeters above the ileocecal valve, which measures 3 centimeters in length and has a square blunt end.

The left kidney is elongated and has the shape of a question mark. It seems to be composed of two leaflike parts; each one has a tube which runs into a common ureter. The right is more rounded and looks like the left with the only difference that it has three parts and three tubes instead of two.

This baby died of acute gastroenterocolitis.

*Autopsy 4177.*—The next case is interesting, for the baby was delivered normally at the obstetrical department of the Philippine General Hospital and after two days showed symptoms of intestinal obstruction. At autopsy there were omental adhesions and marked fibrous adhesions in the peritoneal cavity that bound the coils of intestine to each other and to the peritoneum beneath the umbilicus. The coils of the lower part of the ileum are represented only by a fibrous cord, and the intestinal lumen above this is distended, while the colon has a diameter of only 4 millimeters from serosa to serosa.

#### GASTROINTESTINAL DISEASES

It is a known fact that infant feeding in health or in disease is one of the hardest problems that the pediatrician has to contend with and probably more so in our country where "the milk of beriberic women instead of being a blessing to the child turns to be a curse sometimes." Artificial feeding in the Philippines is difficult, for the poorer class cannot keep the milk on ice, and the temperature favors the development of bacteria in it. The time of weaning is also a period that worries the mother and the

physician because of the lack of suitable domestic infant food. Some mothers go to the extreme of long-continued nursing at the expense of their own health in order to preserve and strengthen, they say, the alimentary tract of their babies, with the result that both mother and child become rachitic. As an example of this, two years ago I was called by a middle-class family to see the youngest child, who was 1 year and 8 months old and entirely breast-fed. The parents told me that the child had an evening rise of temperature and sweating and did not thrive well; physicians had been consulted and oxypathor applied, without any result. I examined the milk of the mother, who was a multipara, and found that it was watery, and by simply giving artificial feeding, the child became well. We have also the other extreme, where young infants are fed with soft-boiled rice, bananas, and almost everything that is found on the family table.

But the worse cases are the children of the poor and ignorant mothers. If the milk is suspected to be the cause of "taol" or infantile beriberi and the mothers are advised to give two teaspoonfuls of condensed milk diluted in boiled water to their infants, they keep giving the same formula for weeks and months, with the result that the child has been probably saved from infantile beriberi to become a victim of malnutrition and finally of gastroenteritis.

Our records contain 207 cases that showed anatomically some lesion in the alimentary tract, without including those due to tuberculosis or Asiatic cholera. The most frequent associated lesions were those of the respiratory tract. Not counting tuberculosis, there were 63 cases of bronchopneumonia, 5 of lobar pneumonia, and 5 with abscesses in the lungs. The next in frequency is otitis media, 15 cases. The lesions as to location in the tract are as follows:

Acute catarrhal gastritis, 9 cases. Four of these were associated with bronchopneumonia, 1 with lobar pneumonia, 1 with chronic colitis, and still another with catarrhal duodenitis and cholecystitis in a burn case.

Gastroenteritis, 26 cases. Twelve of these were chronic and 4 associated with colitis and bronchopneumonia, 7 with bronchopneumonia, 2 with otitis media, and 1 in a male infant of 22 days associated with stomatitis.

Acute enteritis, 38 cases. Six of these were ulcerative, 1 of these being caused by typhoid, and 3 were membranous. Six cases were complicated with bronchopneumonia, 5 with tuberculosis of the lungs, 1 with empyæma, and 1 with suppurative meningitis. One had also oxyuriasis. The last is a 5-day-old

infant with subdural hemorrhage, suppurative pancreatitis, and acute choledochitis. The rest were simple catarrhal inflammations.

**Acute enterocolitis, 51 cases.** Thirty-seven were catarrhal, 14 of which were complicated with bronchopneumonia, 5 with otitis media, 2 with meningitis, with aspiration of food into the lungs, 1 with bronchiectatic abscesses in the lungs and empyæma, and 1 with ischiorectal abscess.

The diphtheritic type of lesion was encountered in 14 cases and the ulcerative in 3 cases. In three instances of the first and one of the latter, which was bacillary, peritonitis was found.

**Chronic enterocolitis, 16 cases.** Five were associated with bronchopneumonia, 2 with miliary tuberculosis, 2 with otitis media, 3 with nephritis, 1 with renal and vesical calculi, 1 with ulcerative colitis, 1 with gastric ulcer, and 1 with malaria.

**Acute colitis, 33 cases.** Thirteen of these were catarrhal, 10 ulcerative, 4 membranous, and 5 ulcerative and membranous. The ulcerative cases were interesting, for they were associated with different lesions, as duodenal ulcer, burn, noma, and peritonitis. Of the latter there were 4 cases, and with bronchopneumonia, 2 cases. All the ulcerative and diphtheritic cases were pure types of bacillary dysentery, 3 of which were associated with bronchopneumonia. Three of the membranous types had pneumonia and 1 tuberculous adenitis. Six cases of the catarrhal type were associated with bronchopneumonia, 1 with lobar pneumonia, 1 with omphalitis, and 2 with otitis media. One of these had also suppurative leptomeningitis. Three cases had nephritis, 1 had duodenal ulcer due to extensive burn, and 1 died due to aspiration of food into the trachea and bronchial tubes.

**Chronic colitis, 34 cases.** Twelve of these were catarrhal, 18 ulcerative, 3 diphtheritic, and 1 amoebic. Six cases of the catarrhal type were associated with bronchopneumonia, 3 with otitis media, 1 with pyæmia, and 1 with tuberculosis. Six of the ulcerative type had bronchopneumonia, 2 otitis media, 1 streptococcaemia, 2 tuberculosis, and 1 inguinal hernia. The description of the lesions in the amoebic colitis is not typical.

In many of these cases of gastrointestinal lesions the diagnosis of malnutrition was encountered.

#### OTHER PATHOLOGIC LESIONS OF THE ALIMENTARY CANAL

Ulcers in the alimentary tract of infants are not rare.

Ulcer of the oesophagus was found in a male, 1 month old, diagnosed clinically as infantile beriberi and confirmed anatomically.

Ulcer of the stomach was met in 3 instances; the first case was a male 25 days old, with the clinical diagnosis of acute gastroenteritis and marasmus and anatomic diagnosis of lobar and lobular pneumonia, acute bronchitis, acute nephritis, and emaciation. The second case was a female 1 year and 6 months old, with chronic gastroenterocolitis, and the third case had ulcerative gastritis and was tuberculous.

Duodenal ulcers, 7 cases. Two of these were due to extensive burns, 1 in a male 5 years old and 1 in a female 1 year old. There is also the record of a case of hemorrhage into the stomach and duodenum with acute bronchopneumonia.

Gall bladder. Besides the congenital anomalies and migration into the gall bladder or into its ducts of parasites, we have 6 cases of catarrhal inflammation. In 1 of these the cholera vibrio was isolated from the gall bladder, and in 2 the lesions seemed to be secondary to those found in the alimentary tract, for in one there was acute diphtheritic enterocolitis with fibrinous peritonitis, and in the other there were hepatic abscesses and tuberculosis of the gastrointestinal tract. The cause of death in 2 was burn and in 1 infantile beriberi.

Perforative diverticulitis was encountered in a boy 4½ years old with acute peritonitis and free *Ascaris* in the peritoneum.

Intestinal obstruction was found once in a girl 25 days old, due to suppurative omphalitis and acute and chronic peritonitis.

The record shows one case of intussusception in a boy 10 months old, who also had generalized tuberculosis. The lower part of the ileum with the base of the appendix formed the intussusceptum and the first part of the ascending colon the intussuscipiens. This series included also a case of megacolon with *Dipylidium caninum*. (34)

#### ASIATIC CHOLERA

As to age, our statistics show that Asiatic cholera attacks all ages and that it increases with age. One premature case lived for six days, and cholera vibrios were found in the intestinal contents after death. The mother of this child had symptoms of abortion for which she was taken and delivered at once in the obstetrical department of the Philippine General Hospital. Soon after delivery they found that the mother was suffering from cholera; she was sent to San Lazaro Hospital, where she died.

August and September have the highest infant mortality record due to cholera, while the record of five years shows its absence during the hot months of April and May (Table I).

TABLE I.—*Infant mortality due to cholera, Manila, 1910–1916.*

Year.	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1910.....	2	1				7	8	12	2	1	1	
1911.....												
1912.....												
1913.....										4	4	3
1914.....	4	1					7	22	26	5	2	2
1915.....	8	1	3									
1916.....		2										
Total.....	9	5	8			7	15	34	28	10	7	5

Our statistics show 103 cases, or 10.3 per cent. We believe that this percentage would have been higher if the intestinal contents had been examined for cholera vibrio in those cases that were diagnosed clinically as cholera infantum and anatomically as acute catarrhal enteritis, especially during epidemics.

McLaughlin, (82) after careful investigation, came to the following conclusions:

Cholera in children is often unrecognized and unreported as such, being reported as acute or chronic enteritis, gastro-enteritis, entero-colitis, dysentery, acute or simple meningitis, and probably also as "infantile" beriberi, convulsions of children, and other diseases. \* \* \*

The clinical picture of cholera in children is often atypical, and the diagnosis may be extremely difficult if not impossible without a bacteriological examination of the intestinal contents. Cerebral manifestations in children suffering from cholera are very common and their severity is in inverse proportion to the age of the child. Acute meningitis is a very rare disease in Manila, in spite of the statistics to the contrary. The percentage of children attacked by cholera is higher than shown by the statistics of the Bureau of Health.

During this last epidemic of cholera (1916), Doctor Crowell ordered that routine examination of the intestines and gall bladders of all autopsies be made. It was found that many children that were clinically diagnosed with some intestinal trouble harbored the cholera vibrio.

TABLE II.—*Age incidence of cholera cases.\**

Months.	Cases.	Years.	Cases.
0 to 1	4	1 to 1½	13
1 to 2	2	1½ to 2	10
2 to 3	3	2 to 2½	15
3 to 4	0	2½ to 3	7
4 to 5	1	3 to 3½	27
5 to 6	3	3½ to 4	5
6 to 7	0	4 to 4½	16
7 to 8	0	4½ to 5	11
8 to 9	2		
9 to 10	1		
10 to 11	1		
11 to 12	1		

\* No age given, 1 case.

In reviewing these records, one's attention is attracted by the great frequency of the association of the disease with *Ascaris lumbricoides* and their migratory activity. In 2 cases they were found in the liver, once in the appendix, twice in the gall bladder, and once in the bile ducts.

In view of the fact that almost all these patients were either taken to San Lazaro Hospital when sick or died in their homes and did not receive treatment for *Ascaris* as did those that came from the Philippine General Hospital, we cannot draw the conclusion that these parasites are one of the predisposing causes, acting either by lowering the vitality of the patient or by disturbing the function of the alimentary tract.

Concomitant anatomical lesions. Bronchopneumonia was found in 14 cases. In 6 cases of miliary tuberculosis the cholera vibrio was found bacteriologically in the intestinal contents. It is well known that the mere presence of these vibrios does not mean that the patients were suffering from cholera.(9)

#### INTESTINAL PARASITES

The tropical climate is a favorable one for the development of intestinal parasites, as, for example, has been demonstrated by Wharton(52) in his study of *Ascaris* eggs, who found that at room temperature ten days are sufficient to develop the freshly laid eggs into embryos. Epstein,(14) in the United States, cultivated the eggs of *Ascaris* and found that the embryo was developed after five weeks, and when fed to children, the ova appeared in the stools after three months.

In our records there are 159 cases, or 15.9 per cent, of infection of the four commonest nematodes—*Ascaris*, *Trichuris*, *Ankylostoma*, and *Oxyuris*, and only 1 case of cestode, *Dipylidium caninum*, which was reported to the Manila Medical Association on November 1, 1915.(34)

Cautley(8) cites that girls are more frequently infected than boys, but our record shows the number of boys (83) to be higher than the number of girls (76).

The migration of these worms, especially that of *Ascaris lumbricoides*, is remarkable. It was found five times in the liver, once in the appendix, twice in the gall bladder, and once free in the peritoneal cavity in a case of perforated diverticulitis.

*Oxyuris* was found once in the appendix in a case of tuberculous colitis.

It seems that their migratory activity is stimulated by an abnormal condition of the bowels, for in those cases where they were found in the gall bladder, liver, and appendix, the patients

died of cholera. The size of the adult parasites being greater than the ampulla of Vater or the appendiceal opening, did they go in when they were young, as believed by Perroncito,(41) has there been a previous dilatation of these ducts before their migration, or were these migrations post mortem?

This migratory activity seems also to be stimulated by hunger of the host; for during my service in the department of medicine, Philippine General Hospital, I used to treat children, and adults as well, with symptoms of peritonitis, who proved to harbor a great number of ascarides, by Murphy's peritonitis treatment and saw the subsidence of the symptoms and passage of the worms without the use of any drug.

Table III shows the kind of worms and varieties affecting individuals by age.

TABLE III.—Age distribution of infection by worms.

Age.	Ce- tode.	<i>Asca- ris alone.</i>	<i>Trichu- ris alone.</i>	<i>Oxyu- ris alone.</i>	<i>Anky- lostoma alone.</i>	<i>Asca- ris and Trichu- ris.</i>	<i>Asca- ris and Oxyu- ris.</i>	<i>Asca- ris and Anky- lostoma.</i>	<i>Asca- ris, Tri- churis, and Anky- lostoma.</i>
<i>Months.</i>									
0 to 1.									
1 to 2.									
2 to 3.									
3 to 4.			2						
4 to 5.									
5 to 6.			1						
6 to 7.			1	1					
7 to 8.			1						
8 to 9.		1	1						
9 to 10.				1			1		
10 to 11.			2						
11 to 12.			1						
<i>Years.</i>									
1 to 1.5.		13	1			2			
1.5 to 2.		12	1						1
2 to 3.		24				7	1		
3 to 4.		24		1		10	2	1	2
4 to 5.		30	2			18			
Total.		1	112	6	1	33	3	1	3

As we see, *Ascaris* is the worm that first invades the human alimentary tract and the one that infests the most, being found alone in 112 cases, and if we include those cases where *Ascaris* was found with other intestinal parasites, the number of children infested will rise to 152, or 95.5 per cent.

Garrison and Llamas(19) found 95 per cent of children in

Manila infected with intestinal parasites. In their examination *Trichuris* was found in 92 per cent, *Ascaris* in 56 per cent, *Ankylostoma* in 11 per cent, *Oxyuris* in 1.33 per cent, and *Taenia* in 0.66 per cent.

Garrison, Leynes, and Llamas(18) give the following age distribution of children below 5 years in Taytay, Rizal Province:

TABLE IV.—*Age distribution of infections.*

Age.	Exam- ined.	Infected.		<i>Ascaris.</i>		<i>Trichuris.</i>		<i>Hookworm.</i>		<i>Strongy- loides.</i>	
		Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.	Number.	Per cent.
Under 2 years.....	73	46	63	89	53.4	22	30.1	0	0	0	0
2 to 4 years.....	100	96	96	87	87	75	75	1	1	2	2.0

#### TUBERCULOSIS

Musgrave and Sison,(37) in their study of 1,000 cases of phthisis among the Filipinos, say that the infection among children probably is much below that in adults, because many die before the first year of life and no doubt before tuberculosis has been contracted or has developed to a degree sufficient for recognition.

In this series tuberculosis has been met in 8 per cent, which is very much lower than that found by Gilman(22) and Andrews(5) in adults.

Tuberculosis in infants is highest in the second year and greatest during the first two years of life, decreasing as age advances as shown in Table V.

TABLE V.—*Age incidence of tuberculosis.*

	Cases.
Premature	1
0 to 1 month	1
1 to 6 months	3
6 to 12 months	18
1 to 2 years	17
2 to 3 years	22
3 to 4 years	12
4 to 5 years	11
Total	80

Our premature case lived for thirty-one days and had tuberculous mesenteric lymphatic glands. Whether this is acquired or is an instance of intrauterine infection, I cannot say. The

intrauterine infection, although rare, has been established according to Holt(27) by various authenticated cases and by the work of Martha Wollstein(53) on tuberculosis of the placenta. Holt mentions the case of a premature infant that lived twenty-one days, born of a mother suffering with advanced tuberculosis, who at the autopsy showed tuberculosis of the endometrium.

The number of cases in which the different organs and lymphatic glands were affected is shown in Table VI.

TABLE VI.—*Organs and lymphatic glands affected by tuberculosis.*

Lungs	58	Jejunum	1
Cervical glands	22	Ileum	32
Bronchial glands	13	Colon	18
Peribronchial glands	38	Appendix	2
Mediastinal glands	9	Rectum	0
Mesenteric glands	42	Liver	24
Retroperitoneal glands	9	Pancreas	2
Meninges	14	Gall bladder	0
Pleura	54	Diaphragm	1
Peritoneum	7	Spleen	28
Omentum	4	Adrenal	3
Pericardium	0	Thymus	3
Ependyma	2	Thyroid	2
Joints	1	Pineal gland	1
Bones	1	Kidneys	1
Reproductive system	0	Ureter	1
Esophagus	0	Brain	4
Stomach	1	Cerebellum	1
Duodenum	0		

Lungs. Of the 58 cases of pulmonary tuberculosis, both lungs were involved in 42. The right was singly affected eleven times, and the left was affected five times.

The type of the lesions indicates a more diffuse and acute process than in adults, and in some instances two or three different types were found. There were 23 cases that showed acute miliary tuberculosis, 10 of which were associated with cavities of the pneumonic type, 12 were lobar, and 7 were lobular.

Chronic type of lesions was found in 16 cases, although in 10 the condition was accompanied by ulcerative lesions. In only one case have I seen calcification, which was that of a girl 11 months old (autopsy 1431), who also had acute miliary pulmonary tuberculosis and otitis media.

Peribronchial lymphatic glands. If we follow Holt's(27) description, he divides these into three main groups: the first are those that surround the trachea; the second, those situated at the bifurcation of the trachea and surrounding the primary

bronchi; while the third follows the course of the bronchi into the lungs. That all these glands may be involved is shown by a case where a localized triangular-shaped tuberculous bronchopneumonia of the left upper lobe of the lung showed enlarged glands all along the course of the bronchi and caseous glands around the trachea and hilum of the left lung only.

As to the rôle played by the bronchial glands, Wollstein(63) found the glands adjacent to the right bronchus the seat of primary lesion in 74 per cent of her cases.

Rothe(45) and Dunn(12) believe that the respiratory tract is the usual entrance of the infection in children.

In this series the cervical and thoracic glands were found macroscopically tuberculous in 82 cases, the mesenteric and retroperitoneal in 51 cases, and both sets in 21 cases.

The aërogenic type of infection in Filipino children is probably also the rule, since artificial feeding with fresh cow's milk or any domestic animal is rare and since tuberculosis among cattle and hogs is reported by Brewer as absent.(7)

TABLE VII.—*Relation of involvement of different organs.*

	Cases.
General miliary	28
Lungs and thoracic lymphatic glands only	13
Lungs and mesenteric glands	2
Lungs and intestine and mesenteric glands	12
Lungs, thoracic glands, and liver	1
Lungs and meninges	1
Lungs, pleura, spleen, and thoracic glands	1
Lungs, glands, and spleen	1
Lungs, pleura, and mesenteric glands	1
Lung (left), mediastinal glands, diaphragm, and spleen	1
Lymphatic glands only	6
Intestines and mesenteric glands	4
Intestines and brain	1
Intestines and peribronchial glands	1
Jejunum alone	1
Thoracic glands and meninges	3
Bones and joints	1
Intestines, healed ulcers	1

Pleura. The pleura showed the miliary form in 8 cases and fibrosis in 42, which is the opposite to the type seen in the lungs.

Alimentary system. The ileum held the first place. The stomach case was a boy 5 years old (autopsy 2524) that died of multiple abscesses of the liver due to *Ascaris* and ulcerative tuberculosis of the stomach and intestines.

The liver, spleen, and kidneys were affected in the miliary form, especially the last, or were also involved in a general

pulmonary tuberculosis. This also is true of the pancreas, adrenals, thymus, thyroid, pineal gland, omentum, and peritoneum.

Only 2 cases of tuberculosis of the brain and meninges were associated with pulmonary tuberculosis, all the rest being accompanied by general miliary tuberculosis. In one of these there was a solitary tubercle in the middle lobe of the right lung with caseous peribronchial and tracheal glands.

Causes of death by age. First year. General miliary tuberculosis, 8 cases; pulmonary tuberculosis, 9 cases; bronchopneumonia, 1 case; beriberi, 1 case.

Second year. General miliary tuberculosis, 11 cases; malaria 2 cases; colitis (bacillary) and bronchopneumonia, 1 case; pyæmia, 1 case; status lymphaticus, 1 case; confluent bronchopneumonia, 1 case; pulmonary tuberculosis, 2 cases; and 1 of canerum oris. One case of general miliary tuberculosis died of cholera, and 1 case of malaria had tuberculosis of the intestine.

Third year. General miliary tuberculosis, 4 cases; burn, 1 case; intestinal tuberculosis, 2 cases; cholera, 3 cases; postoperative (otitis media), 1 case. The last one died of lobar pneumonia and bronchiectatic abscesses of the lungs, the tuberculous ulcers in the intestines having healed when the body came to autopsy. One of the cases of intestinal tuberculosis had a solitary tubercle in the cerebellum.

Fourth year. Generalized miliary tuberculosis, 4 cases; pulmonary tuberculosis, 3 cases; suppurative peritonitis, 1.

Fifth year. Three cases, due to pulmonary tuberculosis, abscess of the liver, and tuberculous meningitis, respectively.

#### INFANTILE BERIBERI

In 1908 infantile beriberi among Filipino infants was confirmed by autopsy,(3) and since the studies on infant mortality of McLaughlin and Andrews,(33) the monograph of Guerrero and Quintos,(25) and the experiments of Andrews,(4) this infantile disease has been accepted as an entity.

Infantile beriberi has been for many years at the head of the list of the causes of infant mortality in Manila. The report of the Philippine Health Service for 1915(43) shows that this disease needs a more careful consideration.

As to its etiology, the local physicians attribute it to the milk of the nursing woman, who is either suffering from beriberi or has it in a latent form.

Andrews(4) thinks that the disease is not due to bacteria in the milk nor to toxins, for the anatomical findings do not agree with any of them, and sustains the former view(33) that milk is

deleterious because of something it lacks rather than because of any harmful constituent. He further states that that something which is lacking is needed for the growth and development of nerves and that beriberi is a nutritional disease.

Darling,(10) in 1914, showed the intimate relationship between scurvy and beriberi in adults as to its etiology and that these and certain other cachexias are the result of the continued use of one-sided and deficient diet.

Hess,(26) in his studies of infantile scurvy in children fed with boiled milk, found that the symptomatology and pathology of this assumes actual relationship to beriberi, which is emphasized by a dietetic test modeled after the tiqui-tiqui treatment of infantile beriberi. He used middlings, the pericarp of wheat.

Beriberi in adults has been reported by Little(30) from countries where rice is not used for diet. Signs of beriberi in puppies were produced by feeding them with beriberi milk by Andrews.(4) Neuritis was produced by Gibson(20) in birds by feeding them with normal human milk along with polished rice, and infantile scurvy by Hess(26) in children by using boiled milk.

Poverty and the so-called deficiency diseases are found in many places, and yet infantile beriberi is met only in beriberi regions. This seems to indicate that the disease is prevalent only in infants nursed by women with an exclusive diet of rice (Well and Mouriquand).(51) If this is not so, can we get the same good results by using middlings, or the extract of tiqui-tiqui, or vice versa, in treating infantile scurvy or infantile beriberi?

Vedder(50) believes that the neuritis-preventing substance is probably an organic base as claimed by Funk and showed that it is not volatile and is destroyed by heat.

Fraser and Stanton(15) and later Grijns(24) also demonstrated that heat destroys the protective power of unpolished rice. Can we produce infantile beriberi by feeding healthy infants with the heated milk of nursing women whose diet is other than unpolished rice or can it be produced by the heated milk of healthy women on exclusive rice diet?

Ingier(28) succeeded in producing scurvy in pregnant guinea pigs by following Holst and Frölich's diet and was able to transmit the disease to their offspring. This experiment is in accord with the experience of the local physicians of the preventive value of changing the rice diet of the pregnant or nursing woman with symptoms of beriberi for mongo, rice polishing, or bread.

But those cases that do not show any symptom of beriberi

during pregnancy or the nursing period and yet in which we see the attacks of infantile beriberi in their offspring or nurslings seem to contradict the findings of Ingier and Goldmann (28) in their experiments. The first found the lesions of scurvy more marked in the skeleton of the mother than in the offspring.

*Seasonal prevalence.*—Table VIII shows that infantile beriberi is more prevalent in September, October, and November, disappearing gradually with the approach of the hot season (April, May, and June), according to Andrews.(4) Our records between January, 1910, and March, 1916, show the following annual and monthly incidence:

TABLE VIII.—*Annual and monthly incidence of infantile beriberi.*

Month.	1910	1911	1912	1913	1914	1915	1916	Total.
January .....	12	—	—	1	1	—	—	14
February .....	35	—	1	—	—	—	1	37
March .....	29	—	—	2	—	—	—	31
April .....	11	—	—	—	—	—	—	11
May .....	—	—	—	1	—	—	—	1
June .....	—	1	—	—	—	—	—	1
July .....	—	—	1	—	1	1	—	8
August .....	7	3	—	—	1	—	—	11
September .....	1	3	—	1	1	—	—	6
October .....	4	1	2	2	1	—	—	10
November .....	6	2	7	—	—	2	—	17
December .....	8	2	3	—	—	1	—	9
Total .....	95	20	7	17	6	5	1	—

As we can see, the only months that are more or less exempted are May, June, and July, which are the beginning of the rainy season and the time when palay, or rice, is planted.

The annual occurrence is not the same, and Albert (2) thinks that this may perhaps be explained by the lack of vitamines in certain foods that is observed in certain periods due to agricultural and economic causes.

If the record of 1910 is not taken, but only those of the following years, the monthly incidence is completely different, and we have January, 2; February, 1; March, 2; April, 0; May, 1; June, 1; July, 3; August, 4; September, 5; October, 10; November, 17; and December, 9; which gives the highest mortality during the wet, moist, and cold months. The infrequency of infantile beriberi of these last years may be due to the fact that even the laity is aware of its symptoms, and artificial feeding is given at once.

TABLE IX.—*Age incidence of infantile beriberi cases.*

	Cases.		Cases.
0 to 1 month	6	8 to 9 months	3
1 to 2 months	56	9 to 10 months	1
2 to 3 months	44	10 to 11 months	2
3 to 4 months	12	11 months to 1 year	0
4 to 5 months	6	1 to 1.5 years	2
5 to 6 months	10	2 years and 7 months	1
6 to 7 months	4	Unknown	1
7 to 8 months	2		
		Total	150

It is plainly shown that the highest incidence is in the first three months of life. The oldest case (autopsy 2869) is that of a girl 2 years and 7 months old; the pathologist (B. C. Crowell) wrote the following note: The hypertrophy and dilatation of the heart was due to infantile beriberi, this being probably a residual of an infantile condition.

Of these 15 cases, 65 cases were clinically diagnosed as infantile beriberi and confirmed at autopsy. The clinical diagnosis of the rest is worthy of note, for almost all of them gave symptoms suspicious of either cerebral or respiratory trouble.

Convulsion, 25 cases; meningitis, 3 cases; eclampsia, 2; acute bronchitis, 25; diphtheria (?), 2; bronchopneumonia, 5; undetermined, 10; no diagnosis, 9; nephritis, 1; chronic gastritis, 1; and status lymphaticus, 1. During my hospital service in pediatrics I was more than once tempted, from the clinical standpoint, to diagnose infantile beriberi as status lymphaticus.

Associated anatomicopathologic lesions. Cholera, 1 case; hyperplasia of the spleen, 6; hyperplasia of the glands, 5; hyperplasia of the thymus, 4; acute nephritis, 3; cloudy liver, 2; cloudy kidneys, 1; patent ductus arteriosus, 2; bronchopneumonia, 1; acute suppurative bronchitis, 1; patent fossa ovalis, 3; cystic ovaries, 1; emphysema, 1; ulcerative colitis, 1; tuberculosis, 1; and enterocolitis, 1.

Pure types of infantile beriberi, that is, dilatation and hypertrophy of the right ventricle of the heart, subserous petechial hemorrhages, more or less oedema of the lungs and congestion of the visceral organs, and subcutaneous and serous transudation of fluid, were present in 132 cases.

The hypertrophy and dilatation of the heart has been a perplexing point to almost all the workers in this disease. According to the transactions of the Second Regional Assembly of Physicians and Pharmacists in the Philippines,(1) Guerrero and

others believe that the degeneration of the vagus nerve is the cause of the cardiac dilatation. Albert thinks that the increase of tone of the vagus or its abnormal irritability is the immediate cause of the hypertrophy and dilatation of the right ventricle, while Villareal mentioned that in Japan Miura laid great emphasis on the increase of the second pulmonic sound in diagnosing cases of beriberi.

Miura(35) explains the condition of dilatation-hypertrophy of the right heart in beriberi as due to a diminution in the mass of the lungs through the raising of the diaphragm and the contraction of the ultimate branches of the pulmonary artery through the action of the beriberi poison; Yamagiva,(54) to the contraction of the pulmonary arterioles. Ogata(38) states that there is no diminution of the lumen of the pulmonary vessels in the said disease, and that, if there is any contraction of these vessels, it is only due to post-mortem rigidity.

Matsuoka,(31) in 1911, studied the pulmonary oedema in beriberi and came to the conclusion that in that disease the condition is due to an early weakening of the left ventricle and that the hypertrophy of the right ventricle found in beriberi favors the raising of the pressure in the pulmonary artery and the occurrence of pulmonary oedema. Later in 1915 the same author, after an exhaustive work on changes in the lungs in beriberi, came to the following conclusions:

1. Although pathognomonic pictures of beriberi lungs are still wanting, they have the following characteristics:
  - a. Diminished air capacity or collapse (in spite of vicarious emphysema in one part), and following generally upon this small volume and sharp margins.
  - b. Especially important is the congestion-oedema; this is not confined to the agonic period, in which there may be paralysis, but a true congestion-oedema. Heart-failure cells are to be found not infrequently. Distinct splenisation is present in marked cases of beriberi.
2. The above-mentioned oedema is of constant occurrence, in many areas circumscribed or diffuse.
3. Besides the ascent of the diaphragm following on paresis, there exist for the explanation of the collapse (of varying degrees) numerous important factors, of which hydrothorax is perhaps the most important.
4. For the setting up of dilatation and hypertrophy of the right heart, congestion and congestion-oedema must work hand in hand with the collapse.

Tadaharu Maruyama(48) thinks that the cause of the nerve and muscle degenerations is probably some poison of the existence of which there is as yet no proof.

Hess(26) believes that the pathogenesis of the cardiac enlarge-

ment in scurvy is an involvement of the vagus and that it is hard to understand the predisposition of the right heart to enlarge unless this is associated with a disturbance of the circulation in the lungs. He mentions also the frequent occurrence of pneumonia in the course of scurvy.

In this series bronchopneumonia was diagnosed as terminal and slight in two cases of infantile beriberi (autopsies 1616 and 1618), and description of the lungs is as follows: (4)

Scattered over the surface are a few darker colored areas which are slightly firmer on section, are not elevated above the surface, do not appear granular, and on slight pressure considerable edema fluid can be expressed.

## **BRONCHOPNEUMONIA**

Disease of the respiratory tract is second in rank in the causes of infant mortality in Manila and first in other big cities (Albert).<sup>(2)</sup>

This vulnerability or weakness is, according to Holt, (27) due to its structure, for the trachea of the young is relatively larger, the bronchi are more numerous and occupy greater space, the air sacs are much smaller, and the interstitial tissue is more abundant; besides that, the capacity of the thorax is encroached upon by the high position of the diaphragm, the large size of the thymus gland, and the frequent distention of the stomach and intestines.

The seasonal and age incidences in this series, which comprises 180 cases, or 18 per cent, without including tuberculosis, is as follows:

TABLE X.—Seasonal incidence of bronchopneumonia cases.

TABLE XI.—*Age incidence of bronchopneumonia cases.*

	Cases.
0 to 1 month	21
1 to 6 months	55
6 months to 1 year	38
1 to 2 years	35
2 to 3 years	17
3 to 4 years	9
4 to 5 years	5
Total	<u>180</u>

The above tables show that the mortality is less during May and that the disease is prevalent throughout the year. They also show that the younger the patient the more fatal is the disease and that its occurrence diminishes inversely with age, which is in accord with textbooks.

The sexes in the series are not equally affected, the male sex predominating, there being 100 males and 80 females.

Seat of lesions. Bronchopneumonia is usually bilateral and is found frequently in the posterior parts of the lungs and many times in the lower lobes. In this series the right lung was singly affected in 23 cases and the left in 12 cases. The left lower lobe is the first in the order of frequency, followed by the lower lobe of the right, then the upper lobe of the same side, and lastly the upper lobe of the left. The middle lobe of the right was found affected alone in one instance.

Associated pathologic lesions. Bronchopneumonia is in many instances terminal, and at autopsy it is not always easy to decide accurately whether the lung lesion preceded the other lesions, as those of the alimentary tract, marasmus, and meningitis, or whether it was secondary to them. This type of lung lesion was found associated with some form of morbid condition of the alimentary tract in 90 cases, 12 being Asiatic cholera, and 2 acute enteritis due to typhoid. Some of these were accompanied by other lesions, as otitis media, 5 cases; fibrinous pleurisy, 4; suppurative meningitis, 1; catarrhal cholecystitis, 2; renal and vesical calculi, 1. Other cases showed 2 or 3 morbid conditions, as otitis media; ulcerative colitis and noma or otitis media; and colitis and chronic leptomeningitis.

As extension downward from diphtheritic tracheobronchitis there were 5 cases, and as extension from some pathologic lesion in the other parts of the lungs, as lobar pneumonia and abscesses, there were 12 cases.

It was also found in 2 cases of pyonephritis, in 5 cases of

meningitis, in 19 cases of otitis media, and in 8 cases of abscesses located in different parts of the body.

Parish<sup>(89)</sup> points to the following factors as causes of the prevalence of respiratory affections among Filipino children.

1. Lack of proper clothing.
2. Lack of protection while sleeping.
3. Cold baths usually taken outdoors, under the faucet many times without drying or friction, thus subjecting the child to shock and chilling.
4. Untreated pertussis and other specific bronchial trouble.
5. Infantile beriberi with deficient heart action.
6. Tachycardia which seems to be the rule among Filipinos. Many of these cases suffer from dyspnoea, perspire easily and very profusely, and are easily affected by drafts.

To these I will add the custom of wrapping the newly born infant with flannel or cotton cloth and not bathing the child until after the first or second months. In some instances bath is given, and in these cases tepid water is used until they are 2 or 3 years old.

#### **LOBAR PNEUMONIA**

The anatomic diagnosis of lobar pneumonia was found in 36 cases only.

The age incidence does not correspond with what is expected, that frequency is in direct proportion with age.

TABLE XII.—*Age incidence of lobar pneumonia cases.*

	Cases.
0 to 6 months	11
6 months to 1 year	5
1 to 2 years	10
2 to 3 years	3
3 to 4 years	5
4 to 5 years	2
Total	36

The youngest is a female 22 days old that had lobar pneumonia of the right upper and inferior lobes. The clinical diagnosis of this was infantile beriberi. Next a male and a female, each 25 days old, both showing acute parenchymatous nephritis.

There is only one case that had pneumonia alba and in whose liver *Treponema pallidum* was demonstrated by Levaditi's method of impregnation. The child was a female 3 months old that died of chronic hemorrhagic internal pachymeningitis.

Site of lesion. The left lower lobe was singly affected in 10 cases, and the left upper was affected only once. The right upper

lobe was affected four times and the lower only once. Combined lesions: The right upper lobe has the most varied combinations—with the left lower lobe twice, with the right middle three times, and with the posterior of the right lower lobe and with the right lower lobe once each. The lower lobes and the right middle were involved only once. As we see, the right middle lobe was not singly affected, but only as an extension from the other lobes of the same side.

Our order of frequency is: Left lower lobe thirteen times; right apex, ten times; right base, five times; left apex and the middle, three times per extensionem. This corresponds with that of Holt.(27)

Freer(16) gives this order of frequency—upper lobes are affected as frequently as the lower: More frequently the right upper and the lower left, the former at least twice as often as the right lower; quite frequently also the middle lobe; not uncommonly both lungs involved. During the first years of life, the upper lobes are more often attacked.

Associated lesions. There were 13 cases with serofibrinous pleurisy, 1 with suppurative pericarditis, and 1 with empyæma. It was associated with some form of gastrointestinal trouble in 15 cases, of Asiatic cholera in 4 cases. One had diphtheria, and in another there was found thrombosis of the longitudinal and lateral sinuses of the head. Five cases had also bronchopneumonia. 3 meningitis, 1 empyæma, and 1 otitis media. The records of 4 cases show hypertrophy and dilatation of the heart, 2 of them being clinically diagnosed as infantile beriberi.

One case had bronchiectic abscesses and suppurative anterior mediastinitis with noma. Two cases had empyæma in the same side as the pneumonic lobe, which was the left lower.

#### MENINGITIS

Meningitis has been a favorite clinical diagnosis in cases dying of convulsion, for frequently the physician is only summoned to see the infant in his last hours, or because many of the diseases of these young beings have a hidden and rapid course.

Our record shows 42 cases, the male sex surpassing the female in number, there being 25 of the former and 17 of the latter. The age incidence shows that even the very young can be affected. The youngest is a 5-day-old female with sacral spina bifida, and the next is another female with ectopia vesicæ, that lived for eight days.

TABLE XIII.—*Age incidence of meningitis cases.*

	Cases.
0 to 1 month	8
1 to 6 months	6
6 to 12 months	9
1 to 2 years	10
2 to 3 years	5
3 to 4 years	5
4 to 5 years	4
Total	42

Types. Tuberculous meningitis is the most frequent type as a rule; yet our record shows 22 cases of suppurative, 16 of tuberculous, and 3 of hemorrhagic pachymeningitis and 1 of chronic leptomeningitis.

The diagnosis of suppurative meningitis has been made many times upon the gross pathological lesions and was found in infants of less than 1 year, except in one instance, and also up to the second year, except in three cases. This finding is in accord with Zap.pert. (55)

Associated pathological lesions. All the cases of tuberculous meningitis were the result of an extension of a generalized miliary tuberculosis, except two, which were associated with pulmonary and glandular tuberculosis.

The suppurative form was associated with bronchopneumonia in 6 cases; in 2 with lobar pneumonia, and in 6 with otitis media; 2 of these were hemorrhagic. The rest had no other recorded marked lesion.

#### TYPHOID FEVER

Although typhoid fever is met with great frequency in adults in Manila, yet this series shows only 3 cases. The youngest is a male infant, 7 months and 20 days old, that had swollen Peyer's patches in the upper part of the ileum; these became pronounced, larger, hemorrhagic, and ulcerated as one approached the ileocecal valve. The solitary lymph follicles were not involved. The spleen was enlarged and soft with increased splenic tissue. The second is a 1-year-old female that had bronchopneumonia, swollen Peyer's patches, enlarged and soft glands, and hyperplasia of the solitary lymph follicles. The intestinal contents were watery and yellowish. The spleen was enlarged, dark colored, and soft. The third is a 5-year-old male with mesenteric lymphadenitis and swollen Peyer's patches.

From this we see the infrequency of typhoid in children below 5 years of age, although Rogers (44) speaks of its frequency in children of India. Domingo (11) found no case under 2 years

and only one from 2 to 5 years in his clinical report of 27 hospital cases.

Typhoid in children has a mild course, and Percy,(40) in his clinical report of 380 cases, did not see any perforation.

Fœtal typhoid has not been reported in Manila as far as we know. The study of Morse(36) is nevertheless worthy of note. He comes to the following conclusions:

Infection of the child from the mother is a frequent, but not an invariable occurrence. The bacilli may pass directly from the maternal into the fœtal circulation. The fœtal form of disease is a general blood infection since the intestines are not functionally active. The most common result is death of the foetus and consequent abortion; but the child may be born alive still suffering from infection and die in a short time because of its feeble resistance. Whether a foetus may recover completely and be born alive and well is not yet established.

Griffith and Ostheimer,(23) in 302 cases of typhoid in children under 2½ years of age, found 2 cases of perforation.

#### MALARIA

In spite of the fact that malaria is prevalent in the tropics and is met with in pregnant women of the Philippine General Hospital,(49) we have no record of an intrauterine infection.

The pathological lesions were similar to those found in adults. In this series 6 cases are found; the youngest is a girl 1½ years old.

#### TUMORS

Six cases of tumors are found in this series: 2 cases of glioma of the eye, 1 of fibromata of the capsule of the liver (autopsy 2057), 1 of adenoma of the intestine, and 1 of neuroblastoma of the adrenal, which was diagnosed macroscopically as tuberculosis. Autopsy 1538 shows enlargement of the pineal gland, measuring 15 by 10 by 3 millimeters, which presses upon the aqueduct of Silvius. In the wall of the intestine is noticed a small grayish red area 1 by 0.5 by 0.5 centimeter, which is firm, and section shows a glistening grayish red surface and definite cellular structure. Beneath the endocardium of the heart, more especially on the left than the right ventricle and also in the muscular wall of the left ventricle, are noticed a few small, firm grayish white areas.

Histological examination shows adenoma of the intestine and cœdematous myoma of the heart. (B. C. Crowell.)

#### SUMMARY

This study on the anatomicopathologic lesions of Filipino children under 5 years shows that:

- (1) Hemorrhage is the most frequent cause of death during

the first few days of life and that the brain and meninges are the favorite seats. Congenital anomalies are also responsible in many instances.

(2) Of the children in this series 15.9 per cent are infected with nematodes, and the frequency of infestation increases as age advances. The first variety that invades the alimentary tract of children and the one that infects the most is *Ascaris lumbricoides*, 95.5 per cent. This worm shows also a great migratory activity, which is probably favored by an abnormal condition of the intestines.

(3) The most frequent concomitant lesion of gastrointestinal disease is bronchopneumonia. In 193 cases the morbid condition was located in the colon in 68 and in both intestines in 54 cases. Amœbic dysentery is very rare in children, there being only one recorded case, and yet the lesions as described are not typical.

(4) Asiatic cholera was nil during April and May, the incidence increasing with age and during epidemics. Newly born infants can be infected during their existence from a mother suffering with the disease.

(5) In infants it is almost the rule for tuberculosis to become generalized rather than localized, the lungs being the commonest seat of lesion and the aërogenic type the most frequent mode of infection. The pericardium, œsophagus, duodenum, rectum, gall bladder, and reproductive system were not affected in this series even in a generalized acute and diffuse infection. Tuberculosis in this series has been found in 80 cases.

(6) Infantile beriberi has been anatomically diagnosed in 150 cases. The literature shows that the disease is met only in infants born of, or nursed by, women on an exclusive rice diet. It is not seen in Manila in the children of foreigners that do not eat much rice. If the neuritis-preventing substance is destroyed by heat, can we produce infantile beriberi by feeding healthy infants with heated milk of nursing women whose diet is other than polished rice or can it only be produced by the milk of healthy women who live exclusively on polished rice?

(a) If the anatomic findings of infantile scurvy are similar to those of infantile beriberi and good results can be expected by the use of middlings in the first and tiqui-tiqui in the latter, would we get the same good results if we change the treatment?

(b) The experiments on scurvy by Ingier and by Goldmann and the findings of Gibson and Concepcion(21) seem to be contradicted by the explanation given by some Japanese and local students of infantile beriberi that the beriberi-preventing prin-

ciple does not pass to the milk to be used by the beriberi infant, which on that account develops the disease, while it is used up by the nursing woman, who does not show any symptoms of beriberi.

(c) This series shows that infantile beriberi is less prevalent during April, May, June, and July and that the age most affected is between 1 and 3 months.

(d) The œdema-congestion of the lung pronounced by Matsuoka as the cause of the dilatation-hypertrophy of the right ventricle offers a new field of investigation in both infantile beriberi and infantile scurvy.

(7) Pneumonia, lobar and lobular, has been met with in 21.6 per cent of this series. If in this we include other diseases of the respiratory tract, we shall probably see that this tract is the most vulnerable place in young children.

(8) Suppurative meningitis has been met with more frequently in the records than tuberculous meningitis and more so during the first two years of life.

(9) Typhoid, malaria, and tumors are rare in children of this series.

(10) The pathological study of this series includes only the causes of stillbirths, of death below the first six days of life, diseases of the gastrointestinal tract, tuberculosis, pneumonias, meningitis, typhoid, malaria, and tumors.

I heartily appreciate the valuable advice and assistance given me by Dr. B. C. Crowell in the study of this series.

#### REFERENCES

- (1) *Actas Memorias y Comm. de la II Asamblea Regional de Medicos y Farmaceuticos.* Tipografia Sto. Tomas (1914).
- (2) ALBERT, JOSE. *Bull. Manila Med. Soc.* (1910), 2, 286.
- (3) IDEM. *Phil. Journ. Sci., Sec. B* (1908), 3, 343.
- (4) ANDREWS, V. L. *Ibid.* (1912), 7, 67.
- (5) IDEM. Cited by Musgrave and Sison.
- (6) BLAND-SUTTON. *Tumours Innocent and Malignant.* 5th ed. Cassell and Company, Limited (1907).
- (7) BREWER, I. C. *Phil. Journ. Sci., Sec. B* (1910), 5, 331.
- (8) CAUTLEY, E. *The Diseases of Infants and Children.* 1st ed. Shaw and Sons, London (1910).
- (9) CROWELL, B. C. *Phil. Journ. Sci., Sec. B* (1914), 9, 361.
- (10) DARLING. *Journ. Am. Med. Assoc.* (1914), 63, 1290.
- (11) DOMINGO, E. *Actas, Memorias y Comm. de la II Asamblea Regional de Medicos y Farmaceuticos.* Tipografia Sto. Tomas (1914).
- (12) DUNN, C. H. *Am. Journ. Dis. Child.* (1916), 11, 85.
- (13) EDITORIAL. *Journ. Am. Med. Assoc.* (1915), 65, 1031.
- (14) EPSTEIN. See 27.
- (15) FRASER and STANTON. See 21.

- (16) FREER, E. See 42.
- (17) FINKELSTONE, B. B., and ELLIS, T. L. *Journ. Am. Med. Assoc.* (1915), 65, 2155.
- (18) GARRISON, LEYNES, and LLAMAS. *Phil. Journ. Sci., Sec. B* (1909), 4, 207.
- (19) GARRISON and LLAMAS. *Ibid.* (1909), 4, 185.
- (20) GIBSON, R. *Ibid.* (1913), 8, 469.
- (21) GIBSON, R. B., and CONCEPCION, I. *Ibid.* (1916), 11, 119.
- (22) GILMAN, P. K. *Ibid.* (1908), 3, 211.
- (23) GRIFFITH and OSTHEIMER. *Am. Journ. Med. Sci.* (1905), 130, 581.
- (24) GRIJNS. See 21.
- (25) GUERRERO, M. S., and QUINTOS, J. *El Beriberi en los Niños de Pecho.* Imp. Lorenzo Cribé, Manila, I. F. (1910).
- (26) HESS, A. T. *Journ. Am. Med. Assoc.* (1915), 65, 1003.
- (27) HOLT. Diseases of Infancy and Childhood. 5th ed. Appleton and Company, New York and London (1910).
- (28) INGIER and GOLDMANN. See 18.
- (29) KNOPFELMACHER, W. See 42.
- (30) LITTLE, J. M. *Journ. Am. Med. Assoc.* (1914), 63, 1287.
- (31) MATSUOKA, Y. *Journ. Path. & Bact.* (1915), 20, 53.
- (32) MC LAUGHLIN, A. J. *Phil. Journ. Sci., Sec. B* (1909), 4, 363.
- (33) MC LAUGHLIN, A. J., and ANDREWS, V. L. *Ibid.* (1910), 5, 162.
- (34) MENDOZA-GUAZON, M. P. *Ibid.* (1916), 11, 19.
- (35) MIURA, M. See 31.
- (36) MORSE. See 27.
- (37) MUSGRAVE and SISON. *Phil. Journ. Sci., Sec. B* (1910), 5, 313.
- (38) OGATA, T. See 31.
- (39) PARISH, REBECCA. *Bull. Manila Med. Soc.* (1910), 2, 247.
- (40) PERCY, K. G. *Boston Med. & Surg.* (1915), 178, 565.
- (41) PERRONCITO. *Le Monde Medical* (1916), Año 26, n. 517, 266.
- (42) PFAUNDLER and SCHLOSSMANN. The Diseases of Children. J. B. Lip-pincot Company, Philadelphia and London (1908).
- (43) Report of the Phil. Health Service (1915).
- (44) ROGERS. Castellani and Chalmers' Manual of Tropical Medicine. 2d ed. William Wood & Co., New York (1913), 1057.
- (45) ROTHE. *Deutsch. Med. Wochenschr.* (1911), 37, 343.
- (46) SCHLOSS, O. M., and COMMISKEY, L. J. J. *Am. Journ. Dis. Child.* (1911), 275.
- (47) SHAW, H. L. K., and WILLIAMS, FRANK J. *New York State Journ. Med.* (1915), 15, 348.
- (48) TADAHARU MARUYAMA. Trans. XVIIth Intern. Congr. Med. London (1913), Ser. 3, pt. 2, 81.
- (49) TOLENTINO, M. *Rev. Filipina de Med. y Farm.* (1914), 5, 1.
- (50) VEDDER, E. B. *Phil. Journ. Sci., Sec. B* (1912), 7, 415.
- (51) WELL, E., and MOURQUAND, G. *Lyon Medical* (1916), 125, 177. Abstract from *Journ. Am. Med. Assoc.* (1916), 67, 473.
- (52) WHARTON, L. D. *Phil. Journ. Sci., Sec. B* (1915), 10, 19.
- (53) WOLLSTEIN, M. *Arch. Int. Med.* (1909), 4, 221.
- (54) YAMAGIVA, K. See 31.
- (55) ZAPPERT. See 42.

## BACTERIOLOGIC INVESTIGATION OF FÆCES AND BILE OF CHOLERA CASES AND CHOLERA CARRIERS

By B. C. CROWELL and JOHN A. JOHNSTON

(From the Department of Pathology and Bacteriology, University of the Philippines, and the Biological Laboratory, Bureau of Science, Manila)

The most important advance in the study of cholera within the past decade has been the recognition of the existence of carriers of the disease. These carriers are individuals who harbor the cholera vibrio while in apparent health; they are of two kinds—"convalescent carriers," who have recovered from an acute attack of the disease, and "contact carriers," who have never had the disease, but have contracted the infestation from contact with others who harbored the organism.

Table I shows the cholera cases and the cholera carriers that have been detected in Manila during the last three years.

TABLE I.—*Cholera cases and cholera carriers in Manila in three years.*

Year.	Persons examined.	Carriers detected.		Cholera cases.	Cholera deaths.
		Number.	Per cent.		
1914.....	37,160	580	1.42	490	272
1915.....	10,440	43	0.41	66	44
1916.....	243,974	1,643	0.67	1,340	513

In Bilibid Prison there was a daily average of about 2,700 prisoners during 1914. Fifty-two cases of cholera with 6 deaths occurred, and 189 carriers were detected; of the 189 carriers, 5 developed the disease in from four to eighteen days after having been detected as carriers.

As in typhoid fever the carrier state in cholera has been shown to be intimately, if not causally, related to the existence of gall bladder infection. Until very recently it has been considered that the infection in cholera was limited to the intestinal tract. It is true that as long ago as 1848 Pirogoff<sup>(87)</sup> described pathologic conditions in the gall bladder in cholera, but the importance of this was not recognized.

The next step was the recognition of the presence of the cholera vibrio in the bile in cholera cases, which has been recorded by numerous workers since 1884. Among these workers may be mentioned Doyen,<sup>(6)</sup> Kelsch and Vaillard,<sup>(27)</sup> Nicati and

Rietsch,(32) Tizzoni and Cattani,(44) Rapchevski,(38) Rekowski and Dzierzgowski,(39) Sawtschenko,(40) Girode,(8) Bruloff,(3) Defressine and Cazeneuve,(5) Kulescha,(29) Greig,(9) and Schöbl.(42) The last three authors have especially emphasized the importance of these findings.

In 430 autopsies on cholera cases Kulescha(29) found cholecystitis forty-two times (10 per cent). In 1908, in 109 cholera cases, he found the vibrio in the gall bladder forty-nine times (46 per cent), and in 1909, in 50 cases, he found it thirty-eight times (76 per cent). Bruloff(3) found the vibrio in the bile of 76 per cent of the cases examined. In 1913 Greig(9) examined the bile in 271 fatal cases of cholera and cultivated the cholera vibrio from 80 of these cases (29.5 per cent). He found naked-eye changes in the gall bladder in 12 of this series (4.4 per cent) and in 10 of the 235 cases (4 per cent) in the post-mortem records at the Medical College, Calcutta. Schöbl(42) found cholera vibrios in the bile of 17 of 39 cholera cases examined (43.5 per cent).

In our own series the cholera vibrio was isolated from the bile in 137 of 212 cholera cases (65.2 per cent) and from the bile when the intestinal contents were negative in 12 cases (5.7 per cent). In 32 cases of cholera carriers detected post mortem we found the cholera vibrio in the bile in 24 cases (75 per cent) and in the bile when the intestinal contents were negative in 14 cases (43.7 per cent).

This finding of ours appears to be important. The fact of the presence of the vibrio in the bile in so large a proportion (65.2 per cent) of cholera cases confirms and extends the work of others. The fact of finding the vibrio in the bile in so many cholera cases(12) when it could not be isolated from the intestine emphasizes the importance of examining the bile as well as the intestinal contents of all suspected cholera cases. This importance is still further emphasized by our finding the vibrio in the bile in 75 per cent of cholera carriers and in the bile alone in 43.7 per cent of 32 carriers.

The detection of cholera carriers after death by such examinations is to be expected in view of the large number of such individuals known to exist where cholera is extant. The presence of the vibrio in the bile in a larger proportion of cholera carriers than in the intestine renders the routine examination of the bile as well as the intestine in all cases where cholera is extant of greater importance. The possibility of detecting carriers in this way, who might otherwise have escaped attention, before the outbreak

of an epidemic may be of value to public-health officials in serving to localize an infected focus and allow intensive sanitary measures to be applied to the place.

There are several possibilities concerning the route by which the vibrio reaches the bile from the intestine. In 1913 Greig<sup>(12)</sup> claimed to have recovered the comma bacillus from the urine of 8 out of 55 cholera cases examined. From this finding he argued that in these cases the disease was a septicæmia. In 1914<sup>(14)</sup> he adduced further evidence to show that the disease is at times a septicæmia by isolating the organism from almost all the organs in different cases after death. In a later article<sup>(15)</sup> he refers to the probable dissemination of the vibrio in the tissues in cholera through the lymph stream rather than through the blood stream. Kulescha<sup>(29)</sup> also believed that the bile infection was of haemogenous origin. In 5 cases Schöbl<sup>(42)</sup> failed to confirm Lief-schütz-Jakowleff's finding of vibrios in the tissues of a stillborn child whose mother had suffered from cholera. In 1910 Kulescha<sup>(29)</sup> investigated the urine of numerous cholera cases and failed to find the vibrio. In the same way Schöbl failed to find the vibrio in the urine in 41 examinations of 27 patients and convalescents. While the evidence is conflicting, it must be admitted that occasionally the disease may be a septicæmia, but that under ordinary conditions the gall bladder is more probably infected through the bile ducts from the duodenum. A few attempts on our part to isolate the cholera vibrio from parts of the body outside the intestine and bile passages have failed.

Küster and Günzler<sup>(30)</sup> note that Goldman had pointed out that charcoal fed by mouth could be recovered through a cholecystectomy wound. Küster and Günzler fed charcoal every two hours for a day before operation and after cholecystectomy recovered the charcoal from the bile.

Kulescha<sup>(29)</sup> recovered the vibrio from the bile in one case one year after the acute attack. The International Sanitary Conference at Paris<sup>(22)</sup> in 1911 reported that the duration of the excretion of cholera vibrios by cholera carriers is as a rule short (two to three weeks), but exceptionally it lasts to twelve months. It was also reported that the excretion is also intermittent and irregular and that there occur vibrio-free intervals up to twenty-one days. The occurrence of these vibrio-free periods in cholera carriers is probably accounted for by the retention of the vibrios in the gall bladder and their irregular release. At times they may be too few in the faeces to be recovered, as they are overgrown by other organisms. This irreg-

ularity not only makes it impossible to detect all carriers in any general bacteriologic survey, but it renders difficult the problem of how long a carrier should be hospitalized or regarded as a potential source of infection. Schöbl states that the administration of bile may facilitate the search for cholera carriers among quarantined persons.

Of 189 carriers detected in Bilibid Prison in 1914, 5 developed the disease in from four to eighteen days after having been detected as carriers. In order to detect carriers who might otherwise escape in the routine examination at the cholera hospital in Manila, a follow-up system has been adopted. Cholera carriers and cases are discharged from the hospital after 3 successive negative examinations of the faeces at 2-day intervals. All cholera carriers and recovered cholera cases are followed to their homes and examined weekly for a period of two months. If they are found positive, they are returned to the hospital. About 27 cases were so returned in eight weeks.

The development of antibodies against the cholera vibrio in cases of cholera appears to be rather inconstant. Agglutinins for the cholera vibrio have been found in the blood of cholera patients by Achard and Bensaude,(1) Haller,(23) Karwacki,(26) Schirnow,(41) Kopp,(28) Svenson,(43) Oya,(35) Greig,(17) and many others. Even when agglutinins are present, they are not in great abundance, as the titer of the serum is in the majority of the cases below 1: 500. Kolle and others have shown that normal sera may agglutinate the cholera vibrio in dilutions up to 1: 20. At any rate, the reaction is of limited diagnostic importance in cases of cholera, for it is usually absent in fatal cases, and the agglutinins do not appear to any extent in the blood until convalescence has commenced.(17) Greig thinks that the reaction may be of value in the prognosis of cholera cases, in as much as he found that agglutinins appeared earlier and in greater amounts in nonfatal cases. He also thinks that the reaction may be a valuable preliminary test in the detection of convalescent cholera-carrier cases.

Another point of undetermined importance in dealing with the cholera epidemics is the significance to be attached to the finding of choleralike vibrios in the stools or tissues of persons under examination. Opinions on this question are not as yet unanimous for lack of positive evidence. These vibrios may have all the characters of the true cholera vibrios save that they are not agglutinated by high-titer cholera-agglutinating serum and do not, when injected intravenously into rabbits, produce

a serum that agglutinates the true cholera vibrio. They are strongly haemolytic and liquefy gelatin faster than do the true cholera vibrios. Such nonagglutinable choleralike vibrios have been found in cases that have no relation to cholera and in true cholera cases either in association with the true cholera vibrio or after the true cholera vibrio has disappeared. Evidence varies as to whether it is possible for the true cholera vibrio to lose its agglutinability; it seems probable that the agglutinogenic capacity of the true cholera vibrio is more constant than its agglutinability.

O'Connell (33) states:

These choleroïd organisms are an extremely interesting phenomenon. Their relationship to true cholera may be said to have been established but not defined. Bacteriologists in service in the Far East have noted their appearance in specimens subjected to microscopical examination immediately before and during cholera epidemics. They are not known where cholera is not or has not been recently. Their morphology and biological characteristics are such that it is impossible to distinguish them from true cholera organisms by microscopic examination. Agglutination is the only test under which their reaction is differentiated from that of the cholera vibrio.

Certain authors, Zlatogoroff (45) and Horowitz, (24) have made the assertion that under certain conditions of growth and environment the cholera organism loses all or some of its typical biological characters, regaining them under certain favorable circumstances. Clinicians in the Philippines have repeatedly made the statement that cholera was endemic, notably Heiser (21) and Clements, (4) although the diagnosis was unconfirmed bacteriologically. Any purely theoretical conjecture such as this, unsupported by exact laboratory evidence, must be set aside, and the final decision must be based on experimental facts with absolute exclusion of possible error. The causal relation between the seasonal outbreaks of cholera in India and the vitality of the cholera vibrio outside the human body has already been demonstrated by Greig.

Few of the known microorganisms in the etiology of human diseases appear to be so variable in their morphology as the cholera vibrio. Ohno (34) has called attention to the striking changes noted in shape and motility in cholera strains, and Hovorka (25) has mentioned the impairment of agglutinability. Such changes as these do not seem to be permanent, and some of the causative factors are known, so that it is possible practically to cause such changes to appear at will.

It has been well established that the reported inagglutinability of certain cholera strains was due to the use of an immune

serum of low potency; also certain strains were found to agglutinate with immune rabbit serum, but not with immune horse serum. Zlatogoroff (45) was able to produce agglutination in an imperfectly agglutinable strain of cholera by repeated passage through animals. On the other hand, McLaughlin and Whitmore (31) were unable to confirm Zlatogoroff's work.

Our own work, based on the study of cases of cholera and cholera carriers after death, will now be presented.

From July, 1915, until the present time the intestinal contents and gall bladder from all autopsies have been examined for cholera vibrios as a routine procedure.

*Technic.*—A loop of small intestine about 0.5 meter from the cæcum was ligatured, severed from its connections, placed in a new, clean, self-sealing jar, and transported to the laboratory for bacteriological examination. In the same way the bile ducts were ligatured and severed, and the gall bladder was removed without opening, placed in another new, clean jar, and transported to the laboratory. The specimen as received at the laboratory was handled with sterile instruments. The outer surface of the intestine was seared with a hot spatula, and with a sterile scalpel an incision was made into the lumen of the gut. If the contents were fluid, 1 cubic centimeter was removed with a sterile pipette and inoculated into a cholera peptone tube. The last drop in the pipette was allowed to fall on a Dieudonné plate and was then spread with a sterile platinum loop. If the fæces were solid, 1 standard loop (4 millimeters) was inoculated into peptone and also smeared on a Dieudonné plate. The same procedure was followed with the gall bladder. These direct plates and peptone tubes were incubated overnight at 37.5° C. In the event of the plate remaining sterile the next morning, the peptone tubes were examined that morning for organisms of suspicious motility and new Dieudonné plates were seeded from those plates with suspicious organisms. Suspicious colonies on Dieudonné plates were picked, emulsified in physiologic salt solution, and tested for agglutination with a cholera-immune goat serum of titer 1: 6000, in dilution of 1: 500.

There have been 269 cases in which there has been reason clinically, anatomically, or bacteriologically to suspect the presence of Asiatic cholera. In 22 of these, vibrios were not found, and 5 cases were known to have been carriers of the vibrios at varying periods before death. These latter 27 cases will be discussed later. Of the remaining 242 cases, 32 were interpreted as cholera carriers and 210 as true cholera cases.

The classification of all of these cases is presented in Table II.

TABLE III.—Classification of cases under consideration.

	I. Intestine +, Bile +	II. Intestine +, Bile -	III. Intestine -, Bile +	IV. Intestine -, Bile -
a... Clinically positive; anatomically positive	Cholera, 72	Cholera, 42	Cholera, 5	Cholera, 2.
b... Clinically suspicious; anatomically positive	Cholera, 25	Cholera, 13	Cholera, 1	Cholera, 2.
c... Clinically positive; anatomically suspicious	Cholera, 9	Cholera, 6	Cholera, 1	Cholera, 2; clinical error, 1.
d... Clinically positive; anatomically negative				Not cholera, clinical errors, 4.
e... Clinically suspicious; anatomically suspicious	Cholera, 4	Cholera, 1	Carriers, 2	Possibly not cholera, 2.
f... Clinically suspicious; anatomically negative	Cholera, 1	0	0	Not cholera, 8.
g... Clinically negative; anatomically positive	Cholera, 1	0	0	0
h... Clinically negative; anatomically suspicious	Cholera, 1	0	0	Probably not cholera, 1.
i... Clinically negative; anatomically enteritis	Cholera, 1	0	0	Cholera, clinical error, 1.
j... Clinically negative; anatomically negative	Carriers, 10; cholera, 4	Carriers, 5; cholera case, 1	0	Cholera, clinical error, 1.
k... Clinically undetermined; anatomically positive	Cholera, 1	0	0	Carriers, 11; cholera case, 1
l... Clinically undetermined; anatomically enteritis	Cholera, 1	0	0	Carriers, 11; cholera case, 1
m... Clinically undetermined; anatomically negative	Cholera, 1	0	0	Cholera, 1
n... Clinically enteritis; anatomically enteritis	Cholera, 2	Cholera, 6	0	Cholera, 1
o... Clinically enteritis; anatomically negative	0	0	0	Cholera, 2
p... Known carriers	0	0	1; carriers, 2.	Carrier, 1.
				4

Note:—"Clinically positive" means in the majority of cases that the vibrios were isolated from the feces before death.

"Clinically suspicious" means that there were symptoms pointing to cholera, but bacteriologic examination had not been made before death.

"Anatomically positive" means that at autopsy the case was declared "possibly cholera" by the pathologist on anatomic grounds.

"Anatomically suspicious" means that at autopsy the case was declared "possibly cholera" or "probably cholera" by the pathologist; when the anatomic picture was obscure, as so often happens in children, in decomposed bodies, and in adults in whom cholera has been superimposed on other extensive disease. [See Crowell, Notes on the diagnosis of Asiatic cholera at autopsy, *This Journal*, Sec. B (1914), 9, 361.]

The cases classified as clinically or anatomically "enteritis" were so diagnosed either during life or at autopsy without reference being made to their possible origin.

"Clinical error" means that the case either was diagnosed clinically as cholera when it proved not to be so, or was not diagnosed cholera when it did prove to be so. Many of these cases were not in hospital, but were sent direct to the morgue for diagnosis from their homes, where they were often seen by a physician only after death.

"Anatomic error" means that the case was undetected as cholera at autopsy. In the majority of cases this was accounted for by the presence of other extensive intestinal diseases, the chief of which was tuberculosis.

## CHOLERA CASES

In the 210 cases of cholera, the cholera vibrio was isolated from both the intestinal contents and the gall bladder in 59.5 per cent (125 cases), from the intestine alone in 34.2 per cent (72 cases), and from the gall bladder alone in 5.7 per cent (12 cases). Combining these figures, we see that the cholera vibrio was isolated from the intestine in 93.7 per cent of the cholera cases and from the gall bladder in 65.2 per cent of the cholera cases.

These figures emphasize the importance of the bacteriologic examination of both the intestine and the gall bladder in cases suspected of harboring the cholera vibrio. The number of cases that would have been declared bacteriologically not cholera following examination of the intestine alone is 5.7 per cent. It is also seen that, in cholera cases, examination of the intestine alone is better than examination of the gall bladder alone by 28.5 per cent.

These facts are summarized in Table III.

TABLE III.—*Bacteriologic examination of 210 cases of Asiatic cholera.*

	Per cent.
Intestine+, bile+	59.5
Intestine+, bile-	34.2
Intestine-, bile+	5.7
Intestine+	93.7
Bile+	65.2

## CHOLERA CARRIERS DETECTED POST MORTEM

Among the 269 cases of which this paper treats, there were detected 32 cases which were diagnosed as cholera carriers after full consideration of all available clinical, anatomic, and bacteriologic data. In none of these cases was there anything clinically or anatomically to indicate that they might have been cholera cases, with one exception. The exception was a poisoning case with an enterocolitis, which aroused the suspicion of cholera in the mind of the pathologist before the history was known.

It is not possible for us to trace possible associations between these carrier cases and known cholera cases.

Considering these 32 cases bacteriologically we find that cholera vibrios were found in both the intestine and gall bladder in 31.2 per cent (10 cases), only in the intestine in 25 per cent (8 cases), and only in the gall bladder in 43.7 per cent (14

cases). Combining these figures it is seen that in 56.2 per cent of the carrier cases vibrios were isolated from the intestine and in 75 per cent from the gall bladder. From these figures we see that in carrier cases, in contrast to what has been shown above in true cholera cases, the vibrios were found in the gall bladder 18.8 per cent more frequently than in the intestine.

These facts are summarized in Table IV.

TABLE IV.—*Bacteriologic examination of 82 cholera-carrier cases detected post mortem.*

	Per cent.
Intestine+, bile+	31.2
Intestine+, bile-	25
Intestine-, bile+	43.7
Intestine+	56.2
Bile+	75

These carrier cases are considered to be of such importance that the main facts concerning them are set forth in Table V.

#### CASES KNOWN TO HAVE BEEN CHOLERA CARRIERS

Five cases which were known to have been cholera carriers have been autopsied. Cholera vibrios had been isolated from the feces of these cases at periods of thirty-seven to one hundred seventeen days before death. Between the time of isolation of the vibrios and death, from 12 to 24 successive negative examinations for the vibrios had been made.

Careful search was made in these cases for some possible hidden focus of cholera infection, and numerous cultures from various parts of the body were made. In 4 of these 5 cases no vibrios were found after death. In the fifth case, which had been positive thirty-seven days before death and had since had 12 successive negative examinations, a cholera vibrio was isolated from the bile and a nonagglutinable vibrio from the jejunum and upper and lower ileum. Liver, spleen, cæcum, and sigmoid showed no vibrios in smears or cultures. This case died of pneumonia and a paratyphoid infection. It is to be noted that the interval between the detection of this case as a carrier and his death was the shortest of any of these cases that were examined. Therefore this is the case in which there was the greatest possibility of finding the organism. The data concerning these cases are presented in Table VI.

TABLE V.—*Cholera-carrier cases detected post mortem.\**

Autopsy No.	Clinical diagnosis.	Duration of illness.	Anatomic diagnosis.	Bacteriologic examination of—		Age.
				Intestine.	Bile.	
4907	Meningeal tuberculosis	2 weeks	General military tuberculosis	+	+	6 months.
5029	do	14 days	Fracture of skull	+	+	28 years.
4961	Pulmonary tuberculosis	37 days	Pulmonary tuberculosis	+	+	23 years.
5022	do	6 months	do	+	+	50 years.
5345	do	2 months	do	+	+	5 years.
5016	do	3 days	Lymphosarcoma of intestine	+	+	40 years.
5393	Typhoid	11 days	Pneumonia	+	+	19 years.
5017	Broncho-pneumonia	5 days	Bacillary dysentery	+	+	2 years.
5163	Lobar pneumonia	16 days	Lobar pneumonia	+	+	6.5 months.
5353	Burn	4.5 hours	Burn	+	+	9 months.
5010	Abcess of liver	20 days	Abcess of liver	+	+	45 years.
6064	Sepicemia	4 days	Ruptured abdominal aneurism	+	+	36 years.
6215	Meningitis	17 days	Meningitis	+	+	21 years.
5389	Chronic nephritis	2 months	Chronic nephritis	+	+	69 years.
5390	Tuberculosis	1.5 years	Tuberculosis	+	+	18 years.
6012	Undetermined	(?)	Enterococcit (poisoning)	+	+	33 years.
6110	Chronic enteritis	2 months	Decomposition	+	+	23 years.
6210	Eatritis	(?)	Tuberculosis	—	—	(?)
6314	Undetermined	(?)	Submersion	—	—	36 years.
6211	Pneumonia (known carrier)	1.5 months	Pneumonia	—	—	26 years.
6212			Cholerakite vibrio.	—	—	
4840	Pulmonary tuberculosis	(?)	Tuberculous enteritis	—	—	22 years.
4849	do	1 year	Malaria	—	—	22 years.
4906	Meningeal tuberculosis	16 days	General military tuberculosis	—	—	1 year.
4997	Pulmonary tuberculosis	1 year	Pulmonary tuberculosis	—	—	19 years.
5346	do	1 year	do	—	—	22 years.
5177	do	1 year	do	—	—	36 years.

5364.	do	2 months	do	
		36 days	Lobar pneumonia	
5361.	Typhoid	28 days	Malaria	
5368.	Accident	5 hours	Accident	
5442.	Malaria	10 days	Malaria	
4942.	Undetermined	3 days	Cirrhosis of liver	
	do	(?)	Cellulitis	
5370.				

\* See note to Table II.

TABLE VI.—Data concerning known carrier cases.

Autopsy No.	Clinical diagnosis.	Anatomic diagnosis.	Age.	Duration of illness.	Interval between detection and death.	Number successive negative examinations.	Bacteriologic examination after death.
5367.	Tuberculosis	Tuberculosis	23	8 months	111	24	Gall bladder, intestine, spleen, blood, and pericardial fluid negative.
5368.	Anæmia	Bacillary colitis	22	9 days	117	17	Gall bladder, jejunum, duodenum, ileum, colon, and liver negative.
5372.	Tuberculosis	Tuberculosis	24	2.5 months	96	21	Spleen, gall bladder, blood, duodenum, jejunum, upper ileum, lower ileum, ascending colon, sigmoid, and appendix negative.
5413.	do	do	47	5 months	111	12	Gall bladder and intestine negative.
5211.	Pneumonia	Pneumonia and typhoid.	26	1.5 months	87	12	Bile positive. From jejunum and upper and lower ileum a nonagglutinable vibrio was isolated. Liver, spleen, cæcum, and sigmoid negative.

## NONAGGLUTINABLE VIBRIOS

Vibrios which were not agglutinable by a standard cholera-immune serum were found in 6 cases. It is very probable that they would have been found in more cases, but special search for them was made only during the latter part of the investigation. The data concerning these cases is presented in Table VII.

TABLE VII.—*Data concerning cases from which nonagglutinable vibrios were isolated.*

Autop-sy No.	Clinical diagnosis.	Anatomic diagnosis.	Bacteriologic examination of—	
			Intestine.	Bile.
4827.	Undetermined.....	Acute cardiac dilatation.	Non agglutinable vibrio.	Cholera vibrio.
5211.	Pneumonia (known carrier).	Pneumonia.....	do.....	Do.
5815.	Cholera.....	Probable cholera.....	do.....	Negative.
5897.	Cardiac disease.....	Tuberculosis.....	do.....	Non agglutinable vibrio.
5410.	Tuberculosis.....	do.....	do.....	Negative.
5429.	Accident.....	Pneumonia.....	do.....	Do.

Since early in 1915 some 30 strains of nonagglutinable vibrios isolated from the faeces and gall bladder of positively known cholera patients and from the faeces of cholera contacts and other persons have been studied definitely to prove, if possible, the true status of the strains—that is, whether or not they were to be regarded as of significance, and if they should prove to be of significance, whether the carriers of the nonagglutinable vibrios should be regarded as a menace to public health.

*Method.*—Specimens were taken by means of sterile cotton swabs on pieces of bamboo. As taken, these were placed in sterile tubes containing about 2 cubic centimeters of 3 per cent agar of —1 reaction to phenolphthalein. When received at the laboratory, 10 cubic centimeters of a double-strength peptone were added, and the tubes were incubated overnight, or about eighteen hours, at 37.5° C. Hanging drops were then made and examined for suspicious motility. Dieudonné plates were seeded from all suspicious tubes, and suspicious colonies were fished at the end of a further 24 hours' incubation; the agglutinability was tested with a dilution of 1: 500 of cholera-immune goat serum, titer 1: 6,000. All of these strains of organisms were tested for their agglutinability, but none gave any reaction. They were then transplanted to pure beef bile with transfers to agar every

three days, and the agglutinability was tested each time. After forty transfers, 8 (6 from faeces of cholera carriers and 2 from cholera cases) of these strains showed prompt agglutination in dilution of 1: 500 of an immune serum by the microscopic method and up to 1: 4,000 by the macroscopic method.

Of these strains but 5 held this apparently acquired property of agglutination for any length of time, the other 3 losing it after cultivation for a period of two months. The strains which now agglutinate do not agglutinate as promptly as they did when the property was first acquired about three months ago, but it is still sufficiently quick to warrant their being classed as true cholera organisms on the basis of agglutination.

The 30 strains studied resembled the true cholera vibrio morphologically; all were monociliate and actively motile. All produced indol in peptone water and typical liquefaction in gelatin and growth on Dieudonné. They differed in that, with the exception of the 8 strains noted, none were agglutinated by a high-titer cholera serum. When injected into guinea pigs they did not produce agglutinin which agglutinated a standard cholera vibrio, except that 2 of the 5 strains, which acquired the agglutinating property, did after this acquisition produce a serum which partially agglutinated a standard vibrio in dilution up to 1:100.

#### CASES IN WHICH CHOLERA VIBRIOS WERE NOT FOUND

Twenty-two cases in which cholera vibrios were not found are included in this study on account of their clinical or anatomic features. In 6 of these it is considered that the patients had cholera in spite of the fact that no vibrios were found in either the intestine or gall bladder. This conclusion is based on the clinical and anatomic features shown in Table VIII. Thirteen cases in which there was some reason either clinically or anatomically to suspect cholera were considered not to be cholera after all data were available. Three cases which were clinically and anatomically suggestive of being cholera were considered, in the light of all the evidence, as probably not cholera, but a definite diagnosis on them is reserved. Greig,(20) in a very recent article, states that in 72 out of 659 cholera cases examined no vibrio was found. He also includes as cholera cases 51 other cases in which only a choleralike vibrio was found. It may be noted that in only 6 of the 221 cases considered cholera did we fail to find the true cholera vibrio. Thirteen cases in our series, which were suspected either clinically or anatomically of being cholera, were eliminated from the list of cholera cases after careful consid-

TABLE VIII.—*Data concerning cases in which no vibrios were found.\**

Group.	Au- topsy No.	Clinical diagnosis.	Anatomic diagnosis.	Age.	Duration of illness.	Hours post- mortem.	Conclusion.
IVa	5894 (4986)	Cholera	Cholera	71 years	9 hours	13	Probably cholera.
	do	do	do	3 years	3 days	18	Do.
IVb	5092 (5132)	Suspect cholera	do	6 years 9 months	10 days	36	Do.
	do	do	do	3 years 7 months	7 days	7	Do.
	6114	Cholera	Possible cholera	30 years	6 days	40	Probably not cholera; extensive decomposition.
IVc	5825	do	Probable cholera	17 years	3 days	26	Looks like cholera.
	5887	do	do	37 years	4 days	18	Do.
IVd	5802 (5833)	do	Mitral endocarditis	45 years	(?)	Not cholera.	
	5468	do	Chirrosis of liver	55 years	6 hours	24	Do.
IVe	5897	Suspect cholera	Tuberculosis	30 years	(?)	11	Do.
	5876	do	Probable cholera	5 years	14 days	17	Probably not cholera.
	5869	do	Possible cholera	1 year	3 days	14	Do.
	5895	do	Anomalous colitis	2 years 5 months	5 months	18	Not cholera.
	5241	do	Bacillary colitis	7 years	(?)	12	Probably not cholera.
	5250	do	Acute cardiac dilatation	22 years	16 hours	8	Pure heart case.
	5820	do	Pulmonary tuberculosis	25 years	do	4	Tuberculous case with heart failure.
IVf	5820	do	Pneumonia	80 years	7 days	15	Not cholera.
	5854	do	Strangulated mesenteric hernia.	23 years	1 day	7	Do.
	5862	do	Typhoid	30 years	(?)	43	Do.
	5821	do	Tuberculosis	20 years	2 days	6	Do.
IVg	5894	Infantile beriberi	Probable cholera	4 months	7 days	19	Probably not cholera.

\* See note to Table II.

eration of all the circumstances. If we have made an error in this, it has been on the conservative side.

Some of the details concerning this group of cases are presented in Table VIII.

The general data concerning all the cases under investigation follow:

TABLE IX.—*Group I. Cases in which the cholera vibrio was isolated from the intestine and the bile.*<sup>a</sup>

Group.	Autopsy No.	Number of cases.	Clinical diagnosis.	Anatomic diagnosis.	Remarks.
Ia		72	Cholera.....	Cholera.....	
Ib		26	Suspected cholera.....	do.....	
Ic		9	Cholera.....	Suspected cholera.....	
Id	5886	1	do.....	Tuberculosis.....	Cholera obscured by tuberculosis at autopsy.
Ie		4	Suspected cholera.....	Suspected cholera.....	
If	5159		do.....	Tuberculosis.....	Cholera obscured by tuberculosis at autopsy.
	5206	2	do.....	Hypernephroma.....	Cholera obscured by tumor at autopsy.
Ig	5299	1	Tuberculosis.....	Cholera.....	Clinically undetected.
	5121		Chronic enteritis.....	Probable cholera.....	Clinically undetected. 4 years old.
	5188		Tuberculosis.....	Acute enteritis.....	Clinically undetected. 3½ years old.
Ih		4	Infantile beriberi.....	Slight enteritis.....	Clinically undetected. 4 years old.
	5856		Typhoid.....	Possible cholera.....	Clinically undetected. 7 years old.
	4907		Meningeal tuberculosis.....	General miliary tuberculosis.....	Carrier case.
	5029		do.....	Fracture skull.....	Do.
	5176		do.....	Intestinal tuberculosis.....	May be a cholera case; 2½ years old; 18 hours' illness.
	4961		Pulmonary tuberculosis.....	Pulmonary tuberculosis.....	Carrier case.
	5022		do.....	do.....	Do.
	5846		do.....	do.....	Do.
	5016		do.....	Sarcoma, intestinal.....	Do.
Ij	5089	14	Typhoid.....	Typhoid.....	Probably a cholera case. 5 years old.
	5803		do.....	Pneumonia.....	Carrier case.
	4947		Acute cardiac dilation.....	Acute cardiac dilation.....	Cholera case; obscured by bismuth at autopsy.
	5018		Chronic ileocolitis.....	Dilated heart, anoxia, etc.	Probably a cholera case; 3½ years old.
	5017		Bronchopneumonia.....	Bacillary colitis.....	Probable carrier.
	5168		Lobar pneumonia.....	Lobar pneumonia.....	Carrier.
	5858		Burns.....	Burns.....	Do.
Ik	5006	1	Undetermined.....	Cholera.....	Cholera case, anatomically undetected.
	4827		do.....	Cardiac dilatation.....	Do.
Im	5858	2	do.....	Tuberculosis.....	

\* See note to Table II.

TABLE X.—*Group II.* Cases in which cholera vibrio was present in the intestine but not in the bile.\*

Group.	Autopsy No.	Number of cases.	Clinical diagnosis.	Anatomic diagnosis.	Remarks.
IIa		42	Cholera .....	Cholera .....	Cholera case.
IIb		18	Suspected cholera .....	do .....	Do.
	4871		Cholera .....	Possible cholera .....	Do.
	4959		do .....	(?)	Do.
IIc	5090	5	do .....	Acute catarrhal enteritis.	Do.
	5091		do .....	do .....	Do.
	5815		do .....	Probable cholera .....	Do.
IId	5161	1	do .....	Typhoid .....	Anatomically undetected.
IIe	4992	1	Suspected cholera .....	Probable cholera .....	Cholera case.
IIIh	4881	2	Ascariasis .....	do .....	Infant; clinically undetected.
III	5009		Mumps .....	do .....	Do.
	4828	1	Marasmus .....	Catarrhal enteritis .....	Do.
	5010		Abscess of liver .....	Abscess liver .....	Carrier case.
	5054		Septicæmia .....	Ruptured abdominal aneurism.	Do.
IIJ	5215	6	Meningitis .....	Meningitis .....	Do.
	5309		Chronic nephritis .....	Chronic nephritis .....	Do.
	5329		Beriberi .....	Beriberi ? .....	Probably a cholera case; 3 months old; 8 days illness.
	5860		Tuberculosis .....	Tuberculosis .....	Carrier.
III	5012	1	Undetermined .....	Acute hemorrhagic enterocolitis.	Carrier-poisoning case.
	4889		Acute ileocolitis .....	Probable cholera .....	Cholera case; infant.
	5007		Acute enterocolitis .....	do .....	Do.
IIIn	5080	5	do .....	Acute enterocolitis .....	Do.
	5052		Gastroenteritis .....	Acute enteritis .....	Do.
	4971		Cholera infantum .....	Acute enterocolitis .....	Do.
	4932		Acute ileocolitis .....	Pulmonary tuberculosis.	Probably cholera case.
IIo	5110	8	Chronic enteritis .....	Decomposition .....	Probably carrier.
	5810		Enteritis .....	Tuberculosis .....	Carrier.

\* See notes to Table II.

TABLE XI.—*Group III. Cases in which cholera vibrio was present in the bile but not in the intestine.\**

Group.	Au-topay No.	No. of cases.	Clinical diagnosis.	Anatomic diagnosis.	Remarks.
IIIa		5	Cholera.....	Cholera.....	Cholera cases.
IIIb	4887	1	Suspected cholera.....	do.....	Do.
IIIc	4866	1	Cholera.....	Possible cholera.....	Do.
IIIf	4942	2	Suspected cholera.....	Cirrhosis of liver.....	Carrier.
	5070		do.....	Suppurative cellulitis.	Do.
IIII	5160	1	Meningeal tuberculosis.	Acute catarrhal enteritis.	Probable cholera case; infant.
	4840		Pulmonary tuberculosis.	Tuberculous enteritis.	Carrier case.
	4849		do.....	Malaria.....	Do.
	4851		do.....	Pulmonary tuberculosis.	May be cholera case.
	4906		Meningeal tuberculosis.	General miliary tuberculosis.	Carrier case.
IIIf	4997	12	Pulmonary tuberculosis.	Pulmonary tuberculosis.	Do.
	5165		do.....	do.....	Do.
	5177		do.....	do.....	Do.
	5244		do.....	do.....	Do.
	5184		do.....	Lobar pneumonia.....	Do.
	5001		Typhoid.....	Malaria.....	Do.
	5388		Accident.....	Accident.....	Do.
	5422		Malaria.....	Malaria.....	Do.
IIII	5295	1	Undetermined.....	Possible cholera.....	Cholera case.
IIIm	5314	1	do.....	Submersion.....	Do.
IIIn	4886	2	Acute ileocolitis.....	Probable cholera.....	Cholera case; infant.
	5147		do.....	do.....	Do.
IIIp	5211	1	Known carrier (pneumonia).	Pneumonia.....	Carrier case.

\* See note to Table II.

## SYNOPSIS

The intestinal contents and the bile of 269 cases of cholera and cholera carriers have been examined. In 212 cases of cholera the vibrio was found in the bile in 65.2 per cent and only in the bile in 5.7 per cent. In 32 cholera carriers detected after death, the cholera vibrio was found in the bile in 75 per cent and only in the bile in 43.7 per cent.

In examining a large series of cholera cases the vibrio may not be recovered from the fæces in a certain number in which it is recovered from the bile. In cholera carriers the vibrio was present in this series in the bile in 10 per cent more cases than in cholera cases and only in the bile in 38 per cent more than in cholera cases. From this the importance of routine examination of both bile and fæces becomes apparent.

Five cases that were known to have been carriers before death were examined after death, and only in the one with the shortest period between detection and death (thirty-seven days) was the vibrio found. In that case the vibrio was isolated from the bile only.

Thirty strains of nonagglutinable vibrios, isolated from the fæces and bile of cholera cases, cholera contacts, and others, have been studied. When first isolated, these were not agglutinated by high-titer cholera-immune serum. By growth in bile 8 of these strains acquired the agglutinability. Five of these 8 strains retained this property, and the other 3 lost it after cultivation for a period of two months.

In 6 cases that were clinically and anatomically cholera, the cholera vibrio was not isolated from either the fæces or the bile. Such cases occur in a large series of cholera cases.

## REFERENCES

1. ACHARD and BENSAUDE. *La Semaine med.* (1897), 151.
2. AMAKO. *Centralbl. f. Bakt., Orig.* (1908), 48, 602.
3. BRULOFF. *Russkyi Vratch* (1910), No. 47, 1821.
4. CLEMENTS. *Phil. Journ. Sci., Sec. B* (1908), 3, 185.
5. DEFRESSINE and CAZENEUVE. *Compt. rend. Soc. biol.* (1912), 72, 983-985.
6. DOYEN. *Arch. Physiol. norm. et pathol.* (1885) (III), 6, 179.
7. FLU. *Geneesk. Tijdschr. Nederl. Indië* (1914), 54, 524.
8. GIRODE. *Compt. rend. Soc. biol.* (1893) (III), 9, 507.
9. GREIG. *Ind. Journ. Med. Research* (1913), 1, 44.
10. IDEM. *Ibid.* (1913), 1, 59.
11. IDEM. *Ibid.* (1913), 1, 65.
12. IDEM. *Ibid.* (1913), 1, 90.
13. IDEM. *Ibid.* (1913), 1, 290.
14. IDEM. *Ibid.* (1914), 2, 1.
15. IDEM. *Ibid.* (1914), 2, 28.

16. IDEM. *Ibid.* (1914), **2**, 608.
17. IDEM. *Ibid.* (1914), **2**, 733.
18. IDEM. *Ibid.* (1915-16), **3**, 442.
19. IDEM. *Ibid.* (1915-16), **3**, 628.
20. IDEM. *Ibid.* (1917), **4**, 651.
21. HEISER. *Phil. Journ. Sci., Sec. B* (1908), **3**, 89.
22. International Sanitary Conference at Paris (1911).
23. HALLER. *Russkyi Vratch* (1905), 689.
24. HOROWITZ. *Centralbl. f. Bakt., Orig.* (1911), **58**, 79.
25. HOVORKA J., and HOFER, B. *Ibid.* (1913), **71**, 103.
26. KARWACKI. *Zeitschr. f. Hyg. u. Infektionskrankh.* (1906), **54**, 39.
27. KELSCH and VAILLARD. *Arch. physiol. norm. et pathol.* (1885) (III), **5**, 341-384.
28. KOPP. *Russkyi Vratch* (1909), 185.
29. KULESCHA. *Klin. Jahrb.* (1910), **24**, 137.
30. KÜSTER and GÜNZLER. *Zeitschr. f. Hyg. u. Infektionskrankh.* (1916), **81**, 447.
31. McLAUGHLIN and WHITMORE. *Phil. Journ. Sci., Sec. B* (1910), **5**, 403.
32. NICATI and RIETSCH. *Recherches sur la cholera.* F. Alcan, Paris (1886).
33. O'CONNELL. *Annual Rep. Health Officer, Port of New York* (1915), 14.
34. OHNO. *Phil. Journ. Sci., Sec. B* (1908), **3**, 341.
35. OYA. *Centralbl. f. Bakt., Ref.* (1903-1904), **34**, 202.
36. PFEIFFER and KOLLE. *Centralbl. f. Bakt., 1. Abt.* (1896), **20**, 129.
37. PIROGOFF. *Die pathologische Anatomie der Cholera u.s.w.* St. Petersburg (1850). (Cited by Kulescha, No. 29.)
38. RAPCHEVSKI. *Vrach* (1886), No. 4, 5.
39. REKOWSKI and DZIERZGOWSKI. *Arch. sci. biol.*, St. Petersburg (1892), **1**, 167.
40. SAWTSCHENKO, I. G. *Vrach* (1893), No. 21.
41. SCHIRNOW. *Russkyi Vratch* (1908), No. 8.
42. SCHÖBL. *Phil. Journ. Sci., Sec. B* (1915), **10**, 11.
43. SVENSON. *Zeitschr. f. Hyg. u. Infektionskrankh.* (1909), **64**, 342.
44. TIZZONI and CATTANI. *Ziegler's Beitr.* (1888), **3**.
45. ZLATOGOROFF, S. J. *Centralbl. f. Bakt., Orig.* (1911), **58**, 14.



PROCEEDINGS OF THE MANILA MEDICAL SOCIETY

REGULAR MONTHLY MEETING, FEBRUARY 13, 1917

The business brought before the society is presented in the secretary's minutes, which follow:

The regular monthly meeting of the Manila Medical Society was held at 8.30 in the evening, February 13, 1917, in the College of Medicine and Surgery, Manila, with Lieut. Col. Winter in the chair and with 36 members and 6 visitors present.

The minutes of the last meeting were read and approved as read.

The secretary read a communication from the Daughters of the American Revolution inviting the members of the society to hear Mrs. Winterhalter's paper on the Navy League, to be given at the Columbia Club Hall on February 19, 1917.

The council recommended the following names for election as active members of the society: Lieut. Col. F. A. Winter, M. C., U. S. Army; Capt. J. M. Willis, M. C., U. S. Army; Dr. Ricardo Fernandez y Asis; and Dr. Harry H. Steinmetz. It was moved, seconded, and carried that the society ratify the recommendation of the council.

The resignation of Prof. F. G. Haughwout as editor of the proceedings of the Manila Medical Society, its acceptance by the president, and the approval by the council were presented to the society. It was moved, seconded, and carried that the resignation of Professor Haughwout as accepted by the president and approved by the council be ratified by the society.

It was moved, seconded, and carried that the resignation of Lieut. Col. S. C. Gurney as a member of the council, because of his departure for the United States, be accepted.

The president appointed the following nominating committee to select the candidates to fill the vacancies in the council made by the expired term of Dr. N. M. Saleeby and the resignation of Lieut. Col. S. C. Gurney:

Dr. Otto Schöbl.      Dr. E. S. Ruth.      Capt. John H. Trinder.

The appointment of Dr. R. B. Gibson by the council as editor of the proceedings of the Manila Medical Society was presented for ratification and approved by the society.

The report of the program committee of the Corregidor meeting on January 6, 1917, was referred by the president to the secretary. The report is as follows:

REPORT OF PROGRAM COMMITTEE APPOINTED BY THE PRESIDENT,  
DECEMBER 9, 1916

On December 10 the program committee, appointed by Dr. B. C. Crowell, met at the College of Medicine and Surgery and accepted the kind invitation of the medical officers stationed at Fort Mills to hold the combined annual and regular monthly meeting of the Manila Medical Society in the recreation room of the post hospital at Corregidor on the evening of January 6, 1917.

Through the concerted action of the various heads of the military service, both at Manila and Corregidor, very obliging arrangements were perfected in which the Quartermaster Corps scheduled the U. S. Army transport *Merritt* for transportation on this occasion.

The distance to Corregidor is approximately 40 kilometers, and it takes about two and one-half hours to make the trip. The program arranged for this time is set forth in General Orders No. 99, Headquarters Manila Medical Society, U. S. Army Transport *Merritt*, dated January 6, 1917, a copy of which is attached hereto.

The courtesies shown upon the arrival at Corregidor readily revealed that every detail had been considered by the hosts in preparing for the event. Special cars were kindly furnished by the Quartermaster Corps, and the crowd was taken to the beautiful, modern, concrete hospital building, the recreation room of which had been so carefully and completely decorated and prepared as to give the feeling of cordial welcome the moment one entered.

The program as indicated in the minutes ended about 11.30 and as many as could make it possible remained at Corregidor for the night, while the rest returned to Manila about 3 o'clock on the morning of the 7th.

H. G. MAUL, *Chairman*,

D. DE LA PAZ,

J. E. REED, Jr.,

*Program Committee.*

The report of the committee on the revision and bringing up to date of the constitution and by-laws of the society, composed of Drs. J. A. Johnston, C. H. Manlove, and R. B. Gibson, was presented and approved as revised by the committee.

The president referred to the secretary the report of the committee on the program for the next three months. The report is as follows:

PROGRAM FOR FEBRUARY, 1917, MEETING

1. The program committee presents the following:

The regular monthly meeting of the Manila Medical Society will be held in the College of Medicine and Surgery, on Monday evening, February 12, at 8.30 in the evening. The topic for discussion will be: Recent advances in the diagnosis and treatment of anterior poliomyelitis. The program will include:

Address. Lieut. Col. Francis A. Winter.

Clinical aspects of anterior poliomyelitis. Maj. Henry H. Rutherford.

The problem from the standpoint of the Public Health Service. Dr. Hugh de Valin.

The bacteriology and serology of anterior poliomyelitis. Dr. John A. Johnston.

Discussions by Drs. N. M. Saleeby, William E. Musgrave, and J. E. Reed, jr.

2. It is requested that in order not to bring this subject before the public, this program be withheld from the newspapers.

C. C. HILLMAN,  
*Captain, Medical Corps, U. S. Army,*  
*Chairman.*

The nominating committee for the election of two councilors reported the names of Dr. N. M. Saleeby for five years and Dr. B. C. Crowell for two years, and their election was voted favorably by the society.

The program for the evening was then carried out.

H. G. MAUL,  
*Secretary-Treasurer,*  
*Manila Medical Society.*

#### SCIENTIFIC PROGRAM

#### PRESIDENT'S ADDRESS

By Lieut. Col. F. A. WINTER

I do not believe that I could better use the brief measure of your time, which is given me, than by taking the opportunity to say a word to you on the subject of Manila as it appears to-day to one who saw it first in 1899, just after the American occupation. The contrast picture is full of interest and instruction.

It was very rightly stated in those days that Manila was a startling demonstration of civic capabilities in the matter of dirt and stinks. It needed but the casual attention of any seeker to get confirmation of this, and a teeming population struggling for existence in a sea of mud, during the rains, with the most meager provision of sanitary systems, fully completes the description.

To one coming here eighteen years later, the evidence of civic betterment is so striking that it brings surprise—I might almost say, disbelief—that one is in the same city. I know of no American city where the streets are cleaner, and I know of none where there are fewer stinks. One notes the reclamation of land, which in the early period was a widespread marsh, and well-graded streets and effective buildings replace holes that were full of mosquito foci.

I might elaborate many points wherein the contrast is equally forcible, but on the doctrine that the proof of the pudding is in the eating, it seems to me that nothing carries so much weight to the observer as the betterment of the people, which is so manifest in every town.

They look better fed, they are patently better clothed, and the general aim of well-being is everywhere in evidence. To see hundreds of young men and boys eagerly taking on the temperate zone baseball and football is a cogent argument of the sound body. It carries by implication that something has happened to supply the vis a tergo which these indulgencies require. All of this spells good food, good water, and immunity from disease.

To you as physicians and sanitarians the city and Government owe no small measure of gratitude for the results attained. Modern civilization has a most intimate relation to the medical man, who by his careful survey plays the pioneer rôle in all the betterments which come with progress. It is surprising how many lions are removed from the path by the silent weapons of our profession, and I know of no place where the open season for lions has been a better one than just here.

In keeping with my desire to avoid encroachment on your time, I beg to say only a word of thanks to you for the honor you have conferred in designating me as your presiding officer. I do not know that material changes of policy in the conduct of the society are at all necessary, but I do think something may be done to limit the amount of time spent in the transaction of business at professional meetings. It shall be my endeavor to effect something along this line. Permit me to thank you for the exhibition of your confidence and toleration.

#### CLINICAL ASPECTS OF ANTERIOR POLIOMYELITIS

By MAJ. H. H. RUTHERFORD

Major Rutherford's paper is a report of a case of unquestioned poliomyelitis in an American child living on the Military Reservation on Corregidor Island, at the entrance to Manila Bay. This is the first case of poliomyelitis occurring in the Philippine Islands that has been reported to the Medical Society and has served to call attention to the fact that sporadic cases are not infrequent here. Peculiar interest attaches itself to the case at Corregidor because of the unknown source of infection. The only possible explanation presupposes a carrier who brought the disease from the United States. (EDITOR.)

## PUBLIC HEALTH ASPECTS OF POLIOMYELITIS

By HUGH DE VALIN

[Abstracted.]

The increase of poliomyelitis and the numerous epidemiological problems which it presents to be solved make it of special interest and concern to health officials. Through experimental studies on the monkey the virus has been demonstrated in the secretions from the mucous membrane of the nasopharynx and intestines of human convalescents and in the secretions from the nasopharynx of healthy persons who have been in more or less intimate contact with poliomyelitis patients. This latter class of individuals constitutes the so-called "healthy carriers" of the disease.

The virulence of the virus, inoculated into monkeys, seems not to be correlated with the severity of the degree of illness of the patient as evidenced by clinical symptoms. The virus may be found on the mucous membrane of the nasopharynx up to six months, though it disappears from the central nervous system within a few days to three weeks after the appearance of the paralysis. In man the few examinations recorded have given positive findings several weeks after recovery, and in one case the virus persisted for five months (Flexner).

The virus presents a marked degree of resistance to drying, to climatic temperature change, and to antiseptic solutions in a strength which may be fatal to ordinary bacteria. Transmission seems possible by dust of rooms of poliomyelitis patients (as the virus has been recovered from this source), as well as by sneezing, kissing, from hands, or from contaminated articles.

Insects such as bedbugs, mosquitoes, and lice have not been shown experimentally to convey the disease; the stable fly (*Stomoxys calcitrans*) has been considered as a possible carrier from monkey to monkey, but later investigations have failed to confirm this. The virus does not seem to be found in the blood of man, as is the case for monkeys, an observation which diminishes the probability of transmission by blood-sucking insects. The fly, cockroach, and other insects may play important rôles as mechanical carriers of the infection. Richardson suggests that the rat may be the chief agent for the spread of this disease as for plague; he gives instances of the occurrence of poliomyelitis where association has been demonstrated between human cases and apparent rat foci. Domestic animals do not seem to be carriers of the virus except possibly in a mechanical way.

Experiments with monkeys have shown that infection can be effected by injection of the virus into the brain tissue, into the subdural space, intravenously, intraperitoneally, and subcutaneously, by rubbing the virus on the uninjured or scarified mucous membrane of the nose, or by feeding massive doses through a stomach tube. However, the natural mode of infection seems to be through the mucous membrane of the nose and throat.

No other disease presents a more widely varying epidemiology than poliomyelitis. From year to year the disease has shown a marked increase in prevalence and extended over greater territory throughout the world. The most extensive outbreaks have occurred in regions with marked seasonal variations, as the northern United States and Europe. This increase in prevalence and distribution of the disease is more pronounced in the United States, statistics for the period 1905-1909 showing that of 8,054 cases the United States contributed 5,514. The Public Health Reports for November 10, 1916, listed 49 states reporting poliomyelitis. The maximum of sporadic and epidemic cases occur during the warm, dry months (from May to November in the northern hemisphere). Where the seasonal change is a matter of rainfall, the disease prevails during the dry season. The recent epidemic in New York reached its crisis on August 12, 1916. These facts point to insect transmission rather than to contact infections, such as characterize measles, diphtheria, whooping cough, scarlet fever, etc. (Frost). A peculiar feature of the outbreak of sporadic cases and epidemics is the frequent lack of apparent connection with previously existing foci, a phenomenon explained probably by the undoubtedly numerous unrecognized cases and "healthy carriers." The incidence as compared with other epidemic diseases of children is small, the case rates per 1,000 of population for 27 states during 1915 varying from 0.001 to 0.116. Epidemics in a community seem to be self-limiting, lasting a few months and then gradually disappearing until at least two years have elapsed. The incidence is noticeably higher in small towns and rural communities than in our large cities. The contagiousness of the disease is not great, as indicated by the low incidence in schools and the occurrence of usually but 1 case in a family. Lavinder reported that out of 7,000 cases in New York 6,748 families were involved, those in which 1 case occurred being 97 per cent of the total. Children under 5 years of age furnish from 50 to 90 per cent of the cases, but as the epidemic advances, the incidence for the higher age groups advances. Cases in adults are rare,

though generally severe. In general the mortality is low—4 to 10 per cent—but in New York last year it was over 25 per cent.

To prevent the spread of the disease, all cases and suspects should be reported to the proper health authorities. Immediate hospitalization of all cases should be enforced; if hospitalization cannot be enforced, it should be at least encouraged. The activity of children should be limited, to guard against the spread of disease through association and contact. If schools have been closed, their reopening should proceed with caution, it being better to begin with those of higher age groups. Cases and persons residing on the premises should be quarantined for at least six weeks from the date of onset; however, individuals over 16 years of age may be moved with proper authorization to other quarters after thorough disinfection of person and clothing, and children may similarly be removed to places where there are no children, provided they are quarantined on the new premises for two weeks and kept under close observation. Under exceptional circumstances wage earners may be released from the above restrictions provided there is no association or contact, direct or indirect, with the cases. Children should be excluded from school for two weeks after the raising of quarantine. Patients should be isolated in screened and bare quarters, and clothing, linen, utensils, and other articles disinfected or burned on removal from the sick room. After removal of the patients the quarters and furniture should be scrubbed and gone over with some disinfectant solution, and carpets, mattresses, and similar articles should be disinfected or, at least, thoroughly exposed to the sun. Animals should be excluded or, if present, be given a disinfecting bath before removal. All faecal and nasopharyngeal discharges should be thoroughly disinfected. Frequent cleansing of the nasopharynx with a weak antiseptic solution, such as hydrogen peroxide, is recommended for patients and contacts. Contact between attendants and outsiders should be limited to essentials. Attendants should not handle food-stuffs for others than the patients, and the distribution of milk or foodstuffs from infected premises should be prohibited. A more or less strict control of travel, especially of children under 16 years of age, by regulations governing inspection, quarantine, and certification is advisable.

The greatest needs to control the spread of poliomyelitis, at least from the sanitarian's viewpoint, are a ready means of diagnosis for all classes of cases and healthy carriers as well and a more exact knowledge of the manner of transmission of

the disease. Until these things come, we must continue to work more or less in the dark and to expend our energies in labors which are probably to a great extent useless.

**A SUMMARY OF THE PRESENT KNOWLEDGE AS TO THE BACTERIOLOGY OF EPIDEMIC POLIOMYELITIS AND THE CYTOLOGY OF THE SPINAL FLUID**

By JOHN A. JOHNSTON

Certain workers recently reported the isolation of a peculiar streptococcus from throats, tonsils, abscesses in tonsils, and from the central nervous system in cases of poliomyelitis.

Paralysis has been produced in animals of various species by intravenous and intracerebral injection of cultures of this organism, and lesions of the gray matter of their nervous system have been demonstrated. From the nervous system of these animals the streptococcus has been isolated in pure culture, while the other tissues were sterile; it is remarkably polymorphous and appears to grow large or small according to the medium in which it is grown, even after passage through a Berkefeld filter.

Using the organism in its large form, paralysis has been consistently produced in animals known to be insusceptible to inoculation with material from epidemic poliomyelitis as heretofore practiced. After paralysis had been produced in a series of three rabbits, the strain caused characteristic paralysis and lesions of poliomyelitis in monkeys. The exact relation of these results to the facts already established as to the etiology of poliomyelitis cannot yet be definitely stated. It appears that the small, filterable organism which has been generally accepted as the cause of poliomyelitis may be the form which this streptococcus tends to take under anaërobic conditions in the central nervous system and in suitable culture media, while the large and more typically streptococcic forms which investigators have considered contaminations may be the identical organism grown larger under suitable conditions.

In November, 1916, Kolmer reported to the Philadelphia County Medical Society that his examination of over 700 specimens of cerebrospinal fluid showed a general increase in the number of cells. In a perfectly clear fluid flowing under increased pressure no unusual or peculiar types of cells were found. He reports finding microorganisms similar to those reported by Flexner and Rosenau, but claims they are not pathogenic and that animal inoculations were without result. He

regards these organisms as of secondary importance, playing a rôle in poliomyelitis similar to those streptococci found in scarlet fever, but which are not regarded as the cause of scarlet fever.

The examination of the spinal fluid in the early days of the disease and especially before the onset of paralysis usually shows an increased cell count with a low or normal globulin content.

At this early stage the polymorphonuclear cells may amount to 90 per cent of the total. Most specimens show lymphocytes and large mononuclear cells almost exclusively.

After the first two weeks the cell count drops to normal or nearly so, and the globulin content is frequently increased.

The examination reveals no specific diagnostic information, but should nevertheless be made, as it is of value as an aid in diagnosis.

#### DISCUSSION

Interest in the discussion centered chiefly in the reports of other cases, which indicate that poliomyelitis is sporadic in the Philippine Islands. Doctor Musgrave saw a case from Cebu in 1911 and reports a second case occurring about the same time as Major Rutherford's. Doctor Saleeby has treated three cases in the last five years. Doctor Reed believes that he has encountered several cases, one of them a Japanese child who was able to walk about until five days before being paralyzed. Doctor Reed calls attention to the fact that peripheral neuritis must be considered in making a diagnosis of poliomyelitis in the Philippines. Doctor Gonzalez reports four cases in his practice; he states that the paralysis associated with beriberi is never as complete as that for poliomyelitis. Major Billingslea saw two cases in the Philippines in 1908 with the typical flaccid paralysis of poliomyelitis; the children were the offspring of white men and native women.

R. B. GIBSON,  
*Editor of the Proceedings,*  
*Manila Medical Society.*



THE PHILIPPINE  
JOURNAL OF SCIENCE  
B. TROPICAL MEDICINE

VOL. XII

MAY, 1917

NO. 3

THE VARYING MORPHOLOGY OF BACILLUS LEPRÆ AND THE  
ROUTINE MICROSCOPIC EXAMINATION OF NASAL  
MUCUS IN LEPERS<sup>1</sup>

By JOHN A. JOHNSTON

(From the Biological Laboratory, Bureau of Science, Manila)

ONE PLATE

In the microscopical examination of several thousand lepers during the past three years I have been very forcibly impressed by the varying morphological appearances presented by the organism in question. In view of these observations an attempt has been made to classify the forms seen into four groups.

1. Classical type.
2. Fragmentary (degenerative) type:
  - (a) Coarse granules.
  - (b) Fine granules.
3. Solid type:
  - (a) Long form.
  - (b) Short form.

4. Nocardial or streptothrical type.

The first group corresponds to the description of the organism as usually given in the standard textbooks (Plate I, fig. c.). In my experience this is most frequently found in comparatively recent lesions, either of the nodular or macular type. However, it may be found occasionally in the site of old lesions which have undergone a retrogressive process, either naturally or during the administration of chaulmoogra oil, and after the period of abeyance has again become active.

The fragmentary type (Plate I, fig. d) is easily seen in recent lesions, although it is nearly always presented in bacteriological

<sup>1</sup> Received for publication April, 1917.

literature as the type of the organism. However, from the large number of examinations that I have made, I think that the form illustrated in Plate I, fig. c, is the true type. The question arises, what significance have the granules? I am not able definitely to answer this, but believe them to be indicative of a degenerative process for the reason that bacilli containing them are rarely found in active lesions, but are much more frequently seen in old inactive nodules or in the lesions of patients undergoing treatment with chaulmoogra oil.

The solid type (Plate I, figs. e, f) is rare, but is to be found in the discharge from an ulcer of the nasal septum or from the margins of chronic ulcers. In the case of the latter, satisfactory specimens may be obtained by the employment of Tschernogabow's technic.<sup>(6)</sup>

The fourth division is believed to be the parent form of *Bacillus lepræ* as ordinarily seen in the tissues and leproma juice (Plate I, figs. a, o, b). I am wholly in accord with the views of Kedrowski<sup>(2)</sup> and Bayon<sup>(1)</sup> that the organism causing leprosy has two stages in its life history: a nocardial or streptothrical nonacid-fast form and a bacillary and acid-fast one.

#### MICROSCOPIC EXAMINATION OF NASAL MUCUS IN LEPERS

Ever since Sticker<sup>(5)</sup> called attention to the presence of leprosy bacilli in smears made from the nasal mucosa, much stress has been laid upon this fact as a means of diagnosis in doubtful cases. Dr. Victor G. Heiser, formerly Director of the Bureau of Health of the Philippine Islands, always laid especial stress on the microscopical examination of nasal mucus in anæsthetic cases of leprosy, but he also laid stress on the fact that an ulcer or its cicatrix should be present at the junction of the bony with the cartilaginous septum. McCoy,<sup>(3)</sup> in an article published in 1915, states:

I would especially emphasize the necessity of being cautious in drawing conclusions from the examination of nasal smears.

From my experience there is nothing to be gained from the examination of nasal mucus when definite clinical lesions are present. In the absence of clinical signs acid-fast bacilli in the nasal mucus should not be regarded as *prima facie* evidence of the existence of leprosy. The individual should be regarded as suspicious perhaps, and repeated examinations should be made, not omitting the examination of the circulating blood by the method of Smith and Rivas<sup>(4)</sup> during febrile paroxysm. This technic should receive far more attention than has hitherto

been given to it. I believe it to be of much greater importance than the examination of the nasal mucus. The authors lay no stress on the fact that to insure success blood specimens should be taken during the febrile paroxysm.

During 1915 I took, or had taken, smears from 1,021 known lepers resident at the Culion Leper Colony and at San Lazaro Hospital, Manila, with results as shown in Tables I to III.

TABLE I.—*Examination at San Lazaro Hospital, Manila.*

Type.	Number.	Typical positive.	Typical positive.	Atypical positive.	Atypical positive.	Continued positive.
			P. cent.		P. cent.	P. cent.
Anæsthetic . . . . .	37	0	0	0	0	0
Nodular . . . . .	37	22	59.45	1	2.70	62.16
Mixed . . . . .	95	64	66.84	3	3.15	60
Total . . . . .	169	76	44.97	4	2.37	47.34

TABLE II.—*San Lazaro and Culion examinations continued.*

Type.	Number.	Typical positive.	Typical positive.	Atypical positive.	Atypical positive.	Continued positive.
			P. cent.		P. cent.	P. cent.
Anæsthetic . . . . .	87	16	18.89	2	2.29	20.68
Nodular . . . . .	255	181	51.37	3	1.17	52.54
Mixed . . . . .	480	188	40.86	11	2.39	43.26
Total . . . . .	802	385	41.77	16	1.99	43.76

TABLE III.—*Examination at Culion Leper Colony, Culion, P. I.*

Type.	Number.	Typical positive.	Typical positive.	Atypical positive.	Atypical positive.	Continued positive.
			P. cent.		P. cent.	P. cent.
Anæsthetic . . . . .	124	16	12.90	2	1.61	14.51
Nodular . . . . .	292	153	52.39	4	1.36	53.76
Mixed . . . . .	555	243	43.60	14	2.52	46.12
Total . . . . .	971	411	42.82	20	2.06	44.88

It will be readily seen from the above tables that in the anæsthetic cases where reliable findings in the nasal mucus would be of decided value only 12.9 per cent gave positive results, while 46 and 52 per cent of the mixed nodular cases gave positive findings. The conclusion may be safely drawn that examination of the nasal mucus is of no value as a routine measure.

**REFERENCES**

1. BAYON, H. *Brit. Med. Journ.* (1911), **2**, 1269.
2. KEDROWSKI. *Zeitschr. f. Hyg. u. Infekt.* (1910), **66**, 1-97.
3. MCCOY, G. *Am. Journ. Trop. Dis.* (1914-15), **3**, 88-97.
4. SMITH, A. J. *Ibid.* (1914-15), **2**, 327-332.
5. STICKER. *Deutsche med. Wochenschr.* (1897), **23**, 219.
6. STITT. *Diagnostics and Treatment of Tropical Diseases.* P. Blakiston's Son & Co., Phila. (1914), 187.

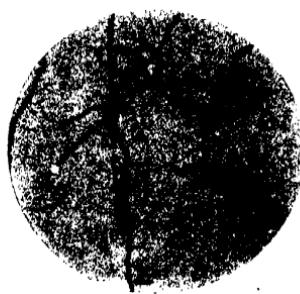
## ILLUSTRATIONS

### PLATE I

Types of *Bacillus lepræ*.

- a* and *b*, nocardial or streptothrical type.
- c*, classical type.
- d*, fragmentary type.
- e*, solid type, long form.
- f*, solid type, short form.





c

d

f

e





# AMOEBOIC ABSCESS OF THE LIVER AMONG FILIPINOS<sup>1</sup>

By RUFINO ABRIOL

(From the Department of Surgery, College of Medicine and Surgery,  
University of the Philippines, and the Philippine General Hospital)

## OUTLINE

- |  |  |
|--|--|
| <p>I. INTRODUCTION.</p> <p>II. ETIOLOGY.</p> <ul style="list-style-type: none"><li>1. Geographical distribution.</li><li>2. Relation to intestinal amoebiasis.</li><li>3. Predisposing factors.<ul style="list-style-type: none"><li>a. Race.</li><li>b. Malaria.</li><li>c. Vicissitudes of temperature.</li><li>d. Seasonal prevalence.</li><li>e. Personal factors.</li></ul></li></ul> <p>III. MORBID ANATOMY.</p> <ul style="list-style-type: none"><li>1. Number of abscesses.</li><li>2. Site.</li><li>3. Size.</li><li>4. Contents of the abscess.</li><li>5. Adhesions.</li></ul> <p>IV. SYMPTOMS.</p> <ul style="list-style-type: none"><li>1. General considerations.</li></ul> | <p>2. Fever.</p> <p>3. Pulse.</p> <p>4. Rigors.</p> <p>5. Sweating.</p> <p>6. Vomiting.</p> <p>7. Pain.</p> <p>8. Cough.</p> <p>9. Blood picture.</p> <p>10. Physical signs.</p> <p>V. DIAGNOSIS.</p> <p>VI. COMPLICATIONS.</p> <p>VII. PROGNOSIS.</p> <p>VIII. TREATMENT.</p> <ul style="list-style-type: none"><li>1. Aspiration.</li><li>2. Rogers's method.</li><li>3. Open operation.<ul style="list-style-type: none"><li>a. Transpleural route.</li><li>b. Abdominal route.</li></ul></li></ul> <p>IX. CONCLUSIONS.</p> |
|--|--|

## INTRODUCTION

Much work has been done on amoebic abscess of the liver by various observers in tropical countries as well as in subtropical and temperate localities; however, as far as I am aware, there is as yet no work presented to the medical world on amoebic abscess of the liver as it exists among the Filipinos. This is explained by the fact that, although the disease is tropical, the majority of its victims are Europeans or other peoples of the white race; hence observers on this disease are amply supplied with material from foreign patients rather than from the natives. The significance and the importance of this affection in the foreign residents in the Philippines have been emphasized by several observers, but as it exists among the Filipinos, little importance is ascribed to it.

<sup>1</sup> Submitted March, 1916, as a thesis for the degree of Doctor of Tropical Medicine. Received for publication April, 1917.

## ETIOLOGY

## GEOGRAPHICAL DISTRIBUTION

Tropical abscess of the liver, another name applied to amoebic abscess of the liver, as the name implies, occurs in the tropics. All authors agree that it is very common in India, Egypt, the Algerian province of Oran,(1) northern and western Africa (Gold Coast), and in Indo-China.(2) It is less prevalent in Ceylon, Malay Peninsula, Java, and Sumatra and is rare in southern China.(2) However, Manson(1) states that amoebic liver abscess along the coast of southern China is a very notable feature of the morbidity of the country. It is rare in Great Britain, and the cases met with occur most frequently in individuals who apparently had acquired the disease in the tropics. Saundby(3) reports a case of liver abscess in England, the patient never having been out of that country. In northern and central Europe it is also rare. Manson,(1) Davidson,(4) and Castellani and Chalmers(2) agree that it is relatively common in southern Europe—in Italy, Greece, the Balkan Peninsula, southern Russia, Spain, and Roumania. Reports of cases in Gibraltar, Malta, and Bengal leave some doubt as to whether or not they were contracted in these stations.(4) In Cyprus, judging from the British colonial reports, it is rare among the natives. For example, in 1908 no cases occurred among 20,000 patients treated, 261 of which were suffering from dysentery.

In Japan, although outside the tropics, it is not uncommon. The population of the southern hemisphere enjoys a practical immunity to the disease, except the Europeans in the warm northern territory of Australia and in the neighboring island of New Caledonia. Corlette(5) reports 7 cases of amoebic liver abscess occurring in New South Wales, the patients having never been outside of Australia. In the Western Hemisphere it is rare in the temperate regions, its prevalence increasing toward the tropics.(1) In the West Indies it is not as common as in India.

It is endemic in the United States. Many authors claim that the cases occurring in the United States were acquired in the tropics, or the intestinal amoebiasis of which liver abscess is a complication can be traced as originating in the warm climates. This is offset by the work of several observers. Osler informs us that it is common in the Southern States. Futch(6) reported 119 cases of amoebiasis occurring in the Johns Hopkins Hospital, 95 of which never had been outside of Maryland. Tuttle(7) showed cases which had never been out of New York.

Boggs<sup>(8)</sup> reported 63 endemic cases in the Southern States. Among other observers corroborating the endemicity in the United States of either intestinal amœbiasis or amœbic abscess of the liver may be mentioned the names of Dock, Libman, and Spelman and Wherry.

There are no data of its occurrence in the Philippines before the American occupation, probably due to the fact that at that time it was not clinically identified and practically no studies on amœbe had been made. Musgrave<sup>(9)</sup> reported 26 cases of amœbic hepatic abscess occurring among foreigners in Manila. Up to 1906 he never saw a case in a Filipino. Strong, McDill, Herzog, Clegg, and Fernandez,<sup>(10)</sup> however, reported a few cases in the natives. Crowell<sup>(11)</sup> reported 9 cases of amoebic abscess encountered in a series of 1,000 autopsies, 6 occurring in Filipinos and 3 in Americans. Gilman,<sup>(12)</sup> in a series of 100 autopsies, encountered it in only 1 subject.

#### RELATION TO INTESTINAL AMŒBIASIS

The intimate relation which exists between dysentery and liver abscess has been pointed out by many observers. Davidson<sup>(4)</sup> says:

Liver abcess is tropical because amoebic liver abscess is confined to the tropics; and its prevalence in a given country or locality is determined by the prevalence and severity of amoebic dysentery in such a country or locality.

With older observers, namely, Prague,<sup>(13)</sup> Altschul,<sup>(13)</sup> Marston,<sup>(18)</sup> Burkhardt,<sup>(18)</sup> Baly,<sup>(18)</sup> and Buchanan,<sup>(18)</sup> during whose time *Amœba* was but little known and neither bacillary nor amœbic dysenteries were clinically well identified, abscess of the liver in numerous autopsies in cases of dysenteries was hardly encountered. Showing the presence of liver abscess in cases of dysentery, Kruse and Pasquale<sup>(18)</sup> found liver abscess in 4 out of 11; Councilman and Lafleur in 6 out of 9; Strong<sup>(14)</sup> in 14 out of 96 autopsies of amoebic colitis; Osler in 23 cases out of 93 amoebic dysenteries; Robinson<sup>(15)</sup> records 12 per cent liver abscess in 96 dysentery autopsies done in the First Reserve Hospital, Manila, in 1899; Futcher<sup>(6)</sup> reports 27 liver abscesses of proved amoebic character out of 119 cases of amoebic dysentery; McDill,<sup>(16)</sup> in a review of over 100,000 cases of dysentery in the eastern countries—70,000 in India—shows 4,000 liver abscess complications. Rogers<sup>(17)</sup> found it in 20 per cent in his large series. Strong and Musgrave<sup>(17)</sup> found liver abscess twenty-three times in 100 fatal cases of amoebic dysentery; these cases were mostly American soldiers. Harris<sup>(17)</sup> found it in 15

out of 95 cases; in Craig's(18) series of 78 fatal cases 33 per cent showed liver abscess, and in his 745 collected cases of amoebic dysentery in which amoebæ were found in faeces 5 per cent showed abscess of the liver. Kartulis,(19) in 500 autopsies, showed 55 per cent amoebic abscess of the liver. Councilman and Lafleur,(19) in their autopsies, numbering 1,429, report 21 per cent with abscess of the liver. Zancarol diagnosed it in 59 per cent of 444 autopsies, Edwards and Waterman(19) in 72.1 per cent out of 699 cases, and Coffin(17) in 34 of 859 cases among American soldiers. Musgrave reports 12 cases out of 100 cases of amoebiasis in St. Paul's Hospital, Manila. McLeod,(20) in 40 cases of amoebic abscess of the liver in Shanghai, had positive evidence of dysentery in all except one, and in this there was no certainty that dysenteric lesions did not exist.

There are latent and marked infections of intestinal amoebiasis(21) which are often overlooked, the patients denying a history of dysentery and presenting no symptoms referable to amoebiasis. Some of these cases go on to recovery or death without ever showing active diarrhoea. Therefore we may have patients who have had no history of dysentery and at the same time have active amoebic lesions in the bowels. Amoebic liver abscess in such subjects gives an impression of having no relation to intestinal amoebiasis. But we must also bear in mind that there may be "individuals who had previously suffered from amoebic colitis, which had finally healed and in which the amoebæ reached the liver during the period of active ulceration of the colon."(9) This might have been a latent form of which the patient knew nothing, and autopsy in fatal cases may show only traces of previous amoebic ulcerations. Rogers(22) calls attention to the fact that amoebic lesions in the bowels may be frequently found post mortem in cases in which there were no symptoms nor history of dysentery during the treatment of the patient for liver abscess. He(22) reports 63 cases of liver abscess of which 35, or 55.5 per cent, had clinical and post-mortem evidence of dysentery; 13, or 20.6 per cent, no history, but with post-mortem evidence of dysentery; 9, or 14.3 per cent, with history, but no post-mortem evidence of dysentery; and 6, or 9.5 per cent, without a history or post-mortem evidence of dysentery. This datum gives us definite evidence of dysentery in 90.5 per cent. In another series of Rogers's(22) of 45 cases 97.8 per cent showed either the presence of active lesions or scars of former dysentery. In a third series, this time clinical cases, Rogers(22) elicited a history of symptoms of dysentery in 72 per cent. Other cases of liver abscess, showing their relation to

dysentery or intestinal ulceration by observers in various countries as tabulated by Davidson,(4) appear below.

TABLE I.—Association of liver abscess with dysentery or intestinal ulceration.

Observer.		Number of cases of abscess.	Cases associated with dysentery or intestinal ulceration.
			Per cent.
1. Annesley	India	29	72.3
2. Waring, E	do	204	72.2
3. Sanitary Commissioners	do	509	53.0
4. Rogers	Calcutta	68	90.48
5. Sacha	Egypt	48	41.7
6. Kartulis	do	500	55 to 60
7. Zancarol	do	444	59.0
8. Kelsch and Kiener	Algeria	500	85.0
9. Smith	Seaman's Hospital	45	84.0

On the other hand, we cannot overlook the remarks of some of the best observers in the world, who have failed to obtain evidence of a dysenteric or amœbic origin of the disease. Musgrave, in his work on amœba and amœbiasis extending for a period of many years, records cases of liver abscess "in which the most careful and persistent search failed to give evidence of a previous dysentery and there was no history of antecedent dysentery or diarrhoea." Morehead(18) failed entirely to discover any intestinal lesion in 21 of his fatal cases of liver abscesses. Kartulis(18) obtained no history, nor did he discover intestinal lesions in 33.3 per cent of his 33 cases. In 7 out of 15 cases Kruse and Pasquale(18) found no lesions in the bowels and obtained no history of dysentery; amœbæ were not identified in the contents of the abscess.

With these data before us, we are led to conclude that there are certain forms of amœbic liver abscess intimately associated with intestinal amœbiasis and that there is another form constituting a small proportion of all cases, which we may consider as a distinct disease. Musgrave(81) contends that amœbiasis of the liver through any channel other than the bowel seems improbable; however, if this be admissible, he offers three possible explanations of the apparent primary infection of the liver: (1) Amœbæ may reach the liver by the gall ducts; (2) they may penetrate the bowel wall without producing apparent lesions; or (3) the bowel lesions may have been entirely repaired.

The first of these propositions is not plausible, when we consider that amoebæ have not been found in the upper part of the intestine and in the gall bladder. However, Dr. B. C. Crowell, of the department of pathology, College of Medicine and Surgery, University of the Philippines, informs us that amoebæ have been found by him in the gall bladder. The second is tenable because Woolley and Musgrave<sup>(23)</sup> have demonstrated that amoebæ may enter the blood vessels early in the disease and may be transported to the submucosa without producing lesions. Many other observers, prominent among whom is Schaudinn,<sup>(24)</sup> corroborate this fact. In the opinion of Musgrave<sup>(23)</sup> the third furnishes the most satisfactory explanation, for it is an established fact that the process of repair, even in very extensive lesions in the intestine, is so complete that traces of the disease cannot be detected macroscopically.

Upon consulting the necropsy records of the department of pathology, College of Medicine and Surgery, University of the Philippines, of 3,630 cases, extending as far back as 1910, I find 83 cases of amoebic colitis among Filipinos, 16 of which were associated with or complicated by liver abscesses. Crowell<sup>(11)</sup> encountered 9 (29 per cent) out of 31 cases of amoebic colitis. Gilman,<sup>(12)</sup> in a series of 100 autopsies, encountered 32 cases of amoebic colitis, only 1 of which was associated with liver abscess.

In reviewing the first 42,246 cases admitted and treated at the Philippine General Hospital, I find 3,561 cases of intestinal amoebiasis, with 99 amoebic liver abscesses. Of the latter cases, 47 were discharged either cured or refusing operation, but with nothing upon which to base the diagnosis except clinical findings and, in some instances, their response to large doses of ipecac and emetine hydrochloride. Fifty-two were proved cases, of which 38 were Filipinos. Of the Filipino cases, 36 were operated upon and 16 died, 12 coming to autopsy. With the exception of 1, all showed ulcerations in the colon. However, the case which showed no lesions in the bowels had symptoms of dysentery while being treated at the hospital and showed amoebæ in the stools. Of these 12 autopsied cases, 5 gave no history of dysentery nor was there any evidence of the disease during life. In our entire series of 38 cases, 26 either gave a history of dysentery or showed evidence of intestinal amoebiasis, while in 12 cases no history of dysentery could be elicited. Four of these 12 died, showing active amoebic lesions in the colon. Therefore we have a total of 30 out of 38 cases, or 79 per cent, with either history or evidence of intestinal amoebiasis.

In regard to the relationship in point of time between the dysentery and the liver abscess, the majority of observers, namely, Musgrave,(9) Rogers,(22) Manson,(1) Davidson,(4) and many others, believe that dysentery antedates the abscess. However, there are cases on record in which the abscess precedes the dysentery. In all of our cases but one, dysentery antedated the abscess where a history or evidences of intestinal amœbiasis were obtainable. In one case the attack of dysentery started at the same time that the symptoms of abscess formation of the liver began.

With reference to the existence of amœbæ in the stools we have 12 cases in our series in which they were found; of these, 9 gave a history of dysentery and 3 denied having had it.

#### PREDISPOSING FACTORS

*Race.*—Practically all observers agree that amœbic liver abscess is more common among foreigners from a cold climate. This fact is hard to explain, especially when we take into consideration that the natives are more susceptible to intestinal amœbic infection. Manson,(1) basing his conclusions on army statistics, places the frequency of liver abscess among Europeans as compared with the natives as 95.2 to 4.8—with amœbic intestinal infection of 43.8 per thousand in the natives and 28.6 in Europeans. Hence natives are more susceptible to intestinal amœbiasis, but to the hepatic infection they are relatively immune,(25) and their immunity diminishes as they come under the influence of urban life. Of 52 cases of amœbic liver abscess, of which I have notes, 38 are Filipinos. The Chinese are much more immune than the natives of the tropics. Musgrave(9) points out that due to their excellent care of food and drink they are immune to amœbiasis. McDill(26) attributes the immunity not only to their habit of eating cooked food, but also to tea drinking.

*Malaria.*—Malaria is mentioned in the etiology of amœbic hepatic abscess, yet all authors of textbooks on tropical medicine agree that it has no influence in its causation. In our series, 12 had remote histories of malaria, but none of the cases had malarial infection at the time of admission to the hospital.

*Vicissitudes of temperature.*—Attention has been called to the comparative rarity(4) of liver abscess in countries where there is hot, moist, and equable climate as compared with other countries where the range of temperature is high and the fluctuations are sudden. Rogers(22) cites the frequency of chilling causing liver abscess, particularly in individuals who have

suffered from dysentery or previous hepatic congestion of the liver. In our series, there are two cases with distinct history of chilling.

*Seasonal prevalence.*—Davidson(4) states that, according to the majority of the Indian authors, liver abscess is most common at the end of the rains and at the beginning of the cold season. Rogers,(27) however, in comparatively recent work on seasonal prevalence of amoebic colitis, concludes that the most frequent occurrence of this intestinal infection is at the beginning of the rainy season. Deeks and Shaw(28) have the same to say in Panama with regard to the prevalence of amoebic colitis. If we take the prevalence of amoebic dysentery as a basis for the occurrence of amoebic liver abscess, we would naturally think that liver abscess would also be more prevalent at the beginning of the rainy season rather than at the end. Table II shows the distribution of our cases by months considered at the onset of the symptoms referable to liver abscess. In the first instance we notice the predominance of the cases during the cool months, that is January and February. With regard to time of onset, we have the majority of the cases during the rainy season.

TABLE II.—*Distribution by months of 38 cases of liver abscess among Filipinos.*

Month.	On admission.	At time of onset of abscesses.
January	4	5
February	7	4
March	1	0
April	1	4
May	8	1
June	8	2
July	2	4
August	3	5
September	5	6
October	5	1
November	3	2
December	1	4
Total	38	38

Dividing our cases into groups representing the admission during periods of three months, or quarterly, we find the same results as obtained in the above table. In the first quarter, the cooler part of the year, we have the majority of the cases at the time of admission and at the time of onset. The predominance is confined to the third quarter, that part of the year with the most rainfall.

TABLE III.—*Quarterly distribution of liver abscess among Filipinos.*

Quarter of year.	On ad- mission.	At time of onset of abscess.
First .....	12	9
Second .....	7	7
Third .....	10	15
Fourth .....	9	7

*Personal factors.*—Liver abscess may occur at any age. Our youngest case was 9 years old and the other extreme was 69 years. It is commonest between the ages of 21 and 40. Among our 38 cases, 22 occurred between these ages. The average age was 36 years and 9 months. Rogers,(22) in a review of 300 cases of liver abscess among Indians and 92 among Europeans, comes to the conclusion that the age incidence among Indians and Europeans is similar. The majority of his cases both in Europeans and Indians was between the ages of 21 and 40. Reports on cases in old age are scanty. Gilman, in 1914 at the December meeting of the Manila Medical Society, reported a case of liver abscess in an Englishman who was 83 years old. Amberg(17) reports 5 cases in children, and Rolleston(18) collected 16 similar cases.

In all endemic regions there is a predominance of cases in men over women. Davidson(4) estimates the proportion of cases in men to women as 30 to 1. The Indian statistics(4) for 1901–3 give the ratio of 7 to 1. Futcher(6) had a ratio of 8 to 1 in his Johns Hopkins series. Many observers claim that women are relatively immune to the disease, because they are less addicted to alcohol and less exposed to other exciting causes of the disease. "Van der Burg(18) ascribes it to menstruation, and this may have a certain influence in diminishing liability to hepatic conditions and indirectly to abscess." If the first argument be tenable, and considering that the Filipino woman of the lower class is as much subject to intemperance and as exposed to other exciting causes of the disease as the man, we may with justice ascribe to this the relative frequency of amœbic liver abscess among Filipino women. In our series, seven occurred in women. This gives us 22.8 per cent of all the cases, and the ratio of the female cases to males is 7:31 or 1:4.43 +.

In the opinion of most observers alcohol, particularly in excess, plays an important rôle in the causation of the abscess, and here we may say that the relative frequency of the disease in Europeans and Americans is ascribed to the fact that they are

more addicted to liquors than the natives. Likewise European women and children are less intemperate, and hence the infrequency of the disease in these individuals. Musgrave<sup>(9)</sup> warns us of giving alcohol a too prominent place in the etiology of liver abscess, basing his conclusions on his series in which alcohol was not an etiological factor. In our series, four gave a history of drinking "vino,"<sup>2</sup> but as all of these except one had a recent history of dysentery, we cannot conclude that alcohol was an etiological factor in these instances.

Excess of animal food and use of hot condiments such as curries and probably pepper are said to contribute, along with other causes, in the formation of liver abscess. Davidson<sup>(4)</sup> states that the influence of excesses of this kind is overestimated, and cites the infrequency of liver abscess among the better class of natives of India who are especially addicted to the vice. All our cases, except one, belong to the middle and lower classes, and we can safely take for granted that gluttony is a rarity, if not absent, among these people.

While in the standard textbooks on tropical diseases no mention is made of the rôle of occupation in the causation of liver abscess, it is of interest to note that 11 of our cases occurred among laborers, 7 among clerks, 4 farmers, 3 soldiers and policemen, 3 housekeepers, 2 fishermen, 2 laundresses, one each in a driver, lawyer, and musician, one in a child, and two without occupation. In connection with amoebic colitis, Deeks and Shaw<sup>(28)</sup> point out that occupation is not an etiological factor, except as it may bring the individual to a position or condition where infected water is solely available for his consumption. In view of this exposure to infection because of occupation, is it not justified to assume that occupation is a factor? Farmers, fishermen, and laborers are the class of Filipinos nearest to nature, and the kind of water available for their consumption is rarely free from amoeba. As already stated, 17 of our cases occurred among these classes of people.

#### MORBID ANATOMY

##### NUMBER OF ABSCESES

The old observers always regarded amoebic abscess of the liver as occurring singly. There is not the slightest doubt that amoebic abscess of the liver may occur in multiple numbers. Craig<sup>(18)</sup> describes cases in which the abscesses could be counted

<sup>2</sup> An alcoholic beverage with about 19 per cent alcohol.

only with great difficulty. Reading the results of various observers, we note that there is a discrepancy in results. Waring,(18) in an analysis of 288 cases, found that 61.5 per cent were single; Niblock,(18) 83 per cent; Rouis,(18) 75 per cent; the Sanitary Commissioner for India in 509 autopsies in 1896-1901 found that only 34 per cent were single. Craig,(18) in an analysis of 24 cases, encountered only 10 single and 14 multiple. In our cases, 6 were multiple and the rest single, the latter giving a percentage of 84.

#### SITE

The majority of our cases are in the right lobe, the upper and lower portions being the favorite seat. Thirty-four cases involved the right lobe. Of these, in 2 the left lobe was also involved and in 1 case the abscesses were distributed throughout all lobes. Two cases were confined in the left lobe. Of those occurring in the right lobe, 10 were in the superior aspect and 11 in the lower part and 13 cases had no definite data as to what part of the right lobe was involved. Rouis,(20) in an analysis of 639 cases, gives the occurrence in the right lobe as 70.85 per cent; in the left lobe as 13.3 per cent; and in the lobus Spigelii as 0.3 per cent. Craig,(28) out of 24 cases, encountered 19 in the right lobe, 8 in the left lobe, and 1 in the lobus Spigelii.

#### SIZE

When we bear in mind that some cases of amœbic abscess of the liver may exist in a person, particularly among the natives, without uncomfortable symptoms, the size of the abscess when it comes to the surgeon's hands must of necessity vary. The abscesses range from 1 millimeter(28) in diameter to one case containing as much as 3,500 cubic centimeters of pus. When multiple, they are generally small. Often two or more abscesses form a single one by confluence. In several of our cases, the abscesses were large enough to yield 2,000 cubic centimeters of pus each.

#### CONTENTS OF THE ABSCESS

The characteristic amœbic pus is diagnostic in itself. Practically in all our cases the pus is viscid and brown in color, resembling thick chocolate. It is odorless and is streaked with blood. The blood may be fresh, being a contamination from the operative incision, or may consist of old clots. Occasionally we may find lumps of translucent mucoid yellowish material which as a rule harbors encysted amœbæ. Microscopically the pus is rich in necrotic liver tissue. Leucocytes, red blood cells, and Charcot-Leyden crystals are also found. Unless there exists a

secondary infection, the pus is bacteriologically sterile. With the presence of bacteria, the color and consistency differ entirely.

In 25 cases in our series the pus was examined and amoebae were identified in 9 cases. *Bacillus subtilis* was present in one case, staphylococci in another; in a third case colon bacillus was present as well as *Oxyuris vermicularis*. Our findings in pure amoebic cases as to the character of the pus correspond very well with the observations of workers in other countries.

#### ADHESIONS

These occur in cases where the abscess is near the surface of the liver. We had one case in which there were so many adhesions around the abscess that during an attempt to separate them the abscess ruptured. In another case the abscess was on the anterior superior surface of the liver, and there were many recently formed adhesions around it, the abscess having ruptured before operation. In spite of the adhesions in this particular case, there was marked secondary peritoneal infection.

#### SYMPTOMS

##### GENERAL CONSIDERATIONS

All observers agree that there are no fixed symptoms which make up a classical clinical picture of amoebic liver abscess. It is true enough that there are certain cases which we can correctly diagnose before operation, but the range of variation of the many clinical signs is so great that experience has compelled us to be more conservative in ascribing the symptoms to liver abscess only. Certain abscesses give typical symptoms of fever, chills, pain, and enlargement of the liver and yet many cases of the large variety show no symptoms whatsoever.

##### FEVER

The fever, just as the symptoms, varies in degree. Four of our cases had perfectly normal temperature; 6 cases had fever ranging from 37° to 38° C. at the time of admission, but twenty-four hours after the patients had been put to bed and proper dieting instituted, the temperature came down to normal. Twelve cases presented an irregular temperature curve, rarely reaching, however, 39.5° C.; 7, with temperature of the remittent type with normal or slightly subnormal in the morning and 37° to 38° C. in the evening; 2 cases with septic temperature; 2 cases with subnormal, 1 remittent and 1 with a continued fever between 37° and 38° C. until twenty-four hours after operation. Musgrave<sup>(9)</sup> states that there is no characteristic fever in liver

abscess; Rogers(22) places the type of fever as remittent in over half of the cases; one seventh, high continued, keeping above 101° F. and varying more than two degrees in the twenty-four hours; in one fifth, the temperature was intermittent; and in 2 out of 57 cases it was normal. While all authors agree that some liver abscesses of the amœbic type at times present no fever, data as to the percentage of the cases in which this exists is not forthcoming except in Rogers's cases cited above. Our Filipino cases of 4 with normal temperature out of 38 cases probably represent the true proportion among the Filipinos.

#### PULSE

The pulse varies according to the degree of temperature present, increasing directly in proportion with the fever.

#### RIGORS

In older descriptions of amoebic liver abscess, rigor is given much prominence. Eleven of our cases gave a distinct history of rigor. This, as a rule, occurred in our cases toward evening as a mild chilly sensation, never so severe as that found in malaria. Slight fever follows it.

#### SWEATING

Rogers(22) and Manson(1) emphasize the presence of copious sweats and state that it may be so abundant as literally to drench the patient's clothes. This particularly occurs when the patient sleeps. In our series four had sweats to a moderate degree, three of the cases were among those who had rigors, and the perspiration occurred immediately after the chill.

#### VOMITING

In regard to vomiting, very little attention is given to it by many observers. Manson(1) attributes it to pressure on the stomach or a catarrhal condition of that organ. In our cases twelve gave symptoms either of nausea or vomiting.

#### PAIN

As to the typical description of the pain referable to liver abscess, Manson(1) says:

There are several types of pain—local and sympathetic—associated with liver abscess. Complaint is almost invariably made of a sense of fulness and of a sense of weight in the region of the liver, not unfrequently referred to the infrascapular region. Stabbing, stitch-like pain, increased by pressure and especially by deep inspiration, by coughing and all sudden jarring movements, is very common, and probably indicates perihepatitis from proximity of the abscess to the surface of the organ. Percussion, or firm palpation, especially if practised during deep inspiration and below

the ribs in front, generally causes smart pain and decided shrinking, the rectus muscle starting up as if to protect the subjacent inflamed parts.

In our series 34 had symptoms of pain in the right hypochondrium; in 1 case in which there was encountered rupture of the abscess into the peritoneal sac, at the time of the operation, the pain was generalized in the abdominal region. In another case in which the location of the abscess was in the right posterior side of the right lobe the pain was in the right side of the chest and in the right shoulder. In a third case the pain was localized in the right iliac region. In this the cæcum was the seat of extensive amoebic lesion; there were multiple abscesses in the right and left lobes, one of the latter having ruptured and formed a subphrenic abscess in the left hypochondrium. In a fourth case the epigastrium and left hypochondrium were the seat of the pain. The abscess in this case ruptured and formed a subphrenic abscess. In one case the onset of the disease started as aching of the long bones. This same patient had his pain in the hepatic region aggravated by ingestion of food.

One frequent symptom in our cases, particularly among those well advanced, was a peculiar sense of fulness in the right upper quadrant of the abdomen. In cases of this kind, as a rule, the patients came to the hospital for no other complaint but this, and they themselves were aware of the presence of a swelling in the upper part of the right side of the abdomen.

#### COUGH

Even in cases uncomplicated by rupture of the abscess into the lungs or actual involvement of the pleura through a process of continuity, cough plays an important rôle in the symptomatology. In abscess of the superior surface of the liver, the irritation on the diaphragm excites a dry, hacking cough. Even in those located in the lower segment of the right lobe, the distension upward may be sufficient to cause coughing. Eight of our cases gave this symptom, three of whom had the abscess in the lower part of the right lobe.

#### BLOOD PICTURE

In cases observed by Manson,(1) Rogers,(22) and Musgrave,(9) no typical blood picture was found. Rogers(22) mentions as high a count as 35,000 and 38,000 leucocytes in two cases, both of the multiple variety. Our case with a count between 25,000 and 30,000 leucocytes was also in a multiple type. Musgrave(9) attributes high leucocytosis to intestinal infection. Table IV shows the leucocytosis in our series.

TABLE IV.—Leucocytosis in liver abscess among Filipinos.

Number.	Cases recovered.	Fatal cases.	Total.
6,000-10,000.....	4	4	8
10,001-15,000.....	9	4	13
15,001-20,000.....	4	5	9
20,001-25,000.....	2	1	3
25,001-30,000.....	1	0	1
(*).....	2	2	4
Total.....	22	16	38

\* Count not made.

We note in this table that eight cases had a count between 6,000 and 10,000, which is practically normal.

Rogers (22) has pointed out that in liver abscess the increase in the polynuclears is less marked than in cases of septic infection.

Table V shows the variation in polynuclear counts in our cases.

TABLE V.—Polymorphonuclear leucocytosis in liver abscess among Filipinos.

Per cent.	Cases recovered.	Fatal cases.	Total.
Less than 60.....	1	0	1
60-65.....	1	0	1
66-70.....	1	0	1
71-75.....	5	1	6
76-80.....	4	1	5
81-85.....	2	5	7
86-90.....	4	3	7
91-95.....	0	2	2
(*).....	4	4	8
Total.....	22	16	38

\* Count not made.

The two cases with counts above 91 per cent may be accounted for in one instance by a colon bacillus infection and in the second by the presence of an independent empyema in the lungs, not secondary to rupture of the abscess. Chalmers and Archibald, (29) in their recent work on the importance of differential counts in uncomplicated intestinal amoebiasis, call attention to the presence of eosinophilia without the presence of worms. The same authors emphasize the mononuclear leucocytosis especially in latent cases as means for diagnosis. If this be the case with uncomplicated cases of intestinal amoebiasis, can we not apply the same principle in hepatic amoebiasis of uncomplicated variety? However, in our series there is only one case

which had an eosinophilic count more than normal, and this showed in the stools the eggs of *Trichocephalus dispar*, *Ascaris lumbricoides*, and *Ankylostoma*. Table VI shows the mononuclear leucocytosis:

TABLE VI.—Mononuclear leucocytosis in liver abscess among Filipinos.

Per cent.	Cases recovered.	Fatal cases.	Total.
0-1.....	13	8	21
2-5.....	3	2	5
6-10.....	1	2	3
11-15.....	0	0	0
16-20.....	1	0	1
(+).....	4	4	8
<b>Total</b> .....	<b>23</b>	<b>16</b>	<b>38</b>

\* Count not made.

#### PHYSICAL SIGNS

The majority of our cases were cachectic, but some of them looked perfectly healthy and well nourished. Marked jaundice was never observed, but a slight yellowish tinge in the conjunctiva was noticed in eighteen cases. Those cases too sick to be about generally lay in bed on the right side with the lower limbs drawn up.

In two of our cases ascites was present, and three had œdema of the legs without nephritis. Two cases presented symptoms of hemorrhoids, and in one case the superficial veins of the anterior abdominal wall were enlarged.

Respiration was proportionate to the fever, if any was present. In those cases with marked pain in the hepatic region, the respiratory movements were limited to the thorax. Auscultation revealed râles or pleuritic rub at the base of the right lung in four cases.

The hepatic dullness varied greatly. In our cases in which abscess was located in the upper segment it reached as high as the fourth rib in the midclavicular line; the lower border was not changed at all in some cases. In abscess of the lower segment of the right lobe the liver becomes prominent in the right hypochondrium. In 27 of our cases there was a definite tumor palpable below the right costal arch. In 2 cases fluctuation was distinct. Tenderness was on the whole very slight except in those cases with mixed infection, and if a moderate or marked degree of abdominal rigidity is present, it is localized in the upper segment of the right rectus.

## DIAGNOSIS

There are certain cases of amœbic liver abscess whose symptoms are so prominent that one can readily make a correct diagnosis. I have already stated that the symptoms of this disease are varied and due to this we are not always in a position to give a correct diagnosis in certain cases. Manson<sup>(1)</sup> puts it thus:

Golden rules in tropical practice are to think of hepatic abscess in all cases of progressive deterioration of health; and to suspect liver abscess in all obscure abdominal cases associated with evening rise of temperature, and this particularly if there be enlargement of or pain in the liver, leucocytosis and a history of dysentery—not necessarily recent dysentery. If doubt exist, there should be no hesitation in having early recourse to the aspirator to clear up diagnosis.

Chief among those diseases which may be confused with liver abscess are syphilitic disease of the liver, cholecystitis and suppurative cholangitis, malarial hepatitis, carcinoma of the liver, pyelonephrosis or hydronephrosis, hydatid cysts, and tuberculous abscess of the abdominal wall. Syphilitic disease of the liver may be excluded by the Wassermann test and therapeutic tests with salvarsan and other antisyphilitic agents. Cholecystitis and suppurative cholangitis are distinguished by high leucocytosis, and in the latter there is apt to be present a distinct septic temperature. The liver, as a rule, is not changed in size. In some of our cases the exclusion of these conditions has not been made before laparotomy was performed. Malarial hepatitis is easily ruled out by the presence of the malarial parasites in the blood and the quick response of the disease to quinine. Carcinoma of the liver has often led us to a mistaken diagnosis. Careful examination shows an enlarged liver of a firm consistency, and sometimes nodules are distinctly palpable. Pyelonephrosis or hydronephrosis, especially when the colon has become adherent to the liver, complicates the diagnosis. Catheterization of the ureters will as a rule lead to their identification. Hydatid cysts are slow in their growth, painless, and devoid of constitutional symptoms. Exploratory puncture may be resorted to in order to observe the character of the fluid in the cavity. Tuberculous abscess of the abdominal wall often leads to a doubtful diagnosis. In some large abscesses of the lower part of the right lobe, particularly when fluctuation is present and when complicated by adhesions of the liver to the parietal peritoneum in a subject with thin abdominal wall, the differentiation is hard to make. Occasionally an abscess of this type

does not move with respiration, and this may be considered a differentiating point. However, exploratory puncture is easily done and settles the diagnosis.

In abscess occurring in the upper segment of the right lobe of the liver, it is natural to assume that the bulging will take place upward, particularly if the location is near the capsule. This, no doubt, explains the relative frequency of the enlargement of the dome as claimed by Osler.(30) The upward enlargement is often hard, if not impossible, to determine by simple percussion. In such cases as these radiography assists very much in ascertaining whether or not there exists an abscess. Of course, any disease that gives rise to an upward enlargement of the liver will lead the radiologist to suspect abscess of the liver; hence the necessity of an experienced eye in interpreting the shadows of the dome of the liver. Fernandez(10) states that abscess in the superior surface of the liver causes a difference in the level of the left and right sides of the diaphragm of 6 to 8 centimeters. Twelve of our cases have been referred to the radiologist for confirmation of the diagnosis. In nine cases a positive diagnosis of liver abscess was reported; in one case, it was probable abscess; in another case, only a statement of enlargement of the liver downward was reported; and in a third case the findings were normal. Among the positive cases, one was of the multiple variety involving the right lobe; three were abscesses of the lower part of the right lobe of fairly large size, probably sufficiently extensive to involve the upper part of the lobe also; and in four cases the lesion was in the dome. The abscess in the doubtful case was in the lower part of the right lobe; the case with a report of enlargement downward presented an abscess in the lower part also; and lastly, the case with normal liver had an abscess in the left lobe.

After analyzing the above results of radioscopy examination of liver abscesses, we cannot accept without question the un-failing value of X-rays as an aid to the diagnosis of liver abscess. However, there is absolutely no doubt that a radiograph, considered in correlation with other symptoms pointing to hepatic abscess, is of great value.

#### COMPLICATIONS

Aside from the colon lesions practically all complications of the liver abscess arise from its spontaneous rupture. Complications which may thus be produced are numerous, their character depending upon the viscera or cavities involved. When the contents of the abscess rupture into the abdominal cavity,

a typical acute peritonitis is produced. Dudley(31) reports a case of this kind with operation and recovery. Rupture into the pleural cavities or pericardium, into the lungs, into the stomach or colon, into the right kidney, and into the portal vessels may take place, giving rise to symptoms referable to the particular structure involved. Cyr(32) gives the results of various observers as follows: Rupture into lung, 59; pleura, 31; pericardium, 1; peritoneum, 39; stomach, 8; intestines, 13; kidney, 2; inferior vena cava, 3; bile passages, 4; externally, 2. Craig,(18) in 7 cases, reported 2 ruptures into the pericardium and 5 into the pleura. In our series 6 of 12 fatal cases had ruptured spontaneously, 4 of these into the peritoneum and 1 into the pleura.

Another peculiar complication of liver abscess is intestinal hemorrhage, ending fatally as a rule. Reports on this complication occur in cases with active lesions in the colon. Strong(33) reports four cases which terminated fatally. Two of our cases presented this complication, one without operation, which ended fatally. In the other case a hemorrhage in the abscess cavity occurred one month after operation, and this was followed twenty-four hours later by hemorrhage from the intestines, about 200 cubic centimeters of bright red blood having been passed per rectum. Elevation of the lower part of the bed, packing the abscess cavity with gauze, administration of emetine hydrochloride intravenously, and subcutaneous injection of normal horse serum saved the patient.

#### PROGNOSIS

Amœbic liver abscess runs a course of varying length. Manson(1) says that generally it is an affair of several months. If proper treatment is instituted early, its course is greatly shortened. If it ruptures, the termination varies with the nature of the visceral involvement. Ruptures occurring into the lungs, stomach, and intestines usually result favorably. At times, small abscesses become encysted or absorbed and thus end in recovery. The coexistence of intestinal amœbiasis, intestinal hemorrhage, broken down state of constitution, and multiplicity of the abscesses add materially to the gravity of the disease. Likewise the existence of mixed infection renders the outlook less favorable.

The death rate among Europeans is high, but is comparatively low among those who come early under observation. Table VII shows a comparison of the percentage of mortality as given by various observers.

TABLE VII.—*Mortality in amoebic liver abscess by various observers.*

Observer.	Cases.	Country.	Mortality. Per cent.
Rouis (1)	208	Algiers	80
Castro (1)	125	Egypt	72.5
Rogers (22)	64	India	53
Megaw (22)	292	India	60.1
Rogers (22)	52	India	73
Abriol	38	Philippines	31.5

We note that the mortality among the 38 cases of Filipinos is relatively low, in spite of the fact that most of our cases come under observation at a very late stage of the disease and many of them are not by any means in a favorable condition for surgical intervention. It is hoped that with the growing popularity of operative procedures among the natives we will be able to reduce the death rate to a very low minimum.

#### TREATMENT

When the diagnosis of amoebic hepatic abscess is definitely established, the treatment resolves itself into various methods of surgical procedure. These range from a simple aspiration and injection with quinine to freely opening and draining the abscess.

#### ASPIRATION AND INJECTION OF QUININE WITHOUT DRAINAGE

Rogers in 1902 was the first to suggest aspiration and injection of quinine without drainage. Later Wilson,(34) Spencer,(34) O'Kenealy,(34) and Stevens(34) reported favorable results from this procedure. Rogers(22) describes the technic as follows:

In carrying out this plan of treatment the following points require attention. The skin at the seat of puncture must be most thoroughly sterilized to prevent any bacteria being carried into the cavity. If the presence and position of the abscess are accurately known a full sized aspiration trocar should be used to allow as much as possible of the thick pus being withdrawn through it. For the same reason it is also an advantage to use a T tube of large calibre fitting into the exhausted bottle. Messrs. Down Bros. have made a suitable one for me. The cavity is emptied as far as possible, some of the first pus being run directly into a sterile test tube for bacteriological examination. A previously boiled solution of the very soluble bihydrochlorate of quinine, of a strength of 10 grains in 1 oz. of water, is now injected into the abscess cavity through the cannula by means of a sterile syringe, and the cannula is then withdrawn

and collodion applied externally. If only a few ounces of pus are obtained, it will be sufficient to inject 2 oz. of the quinine solution, but if a pint or more is present then 4 oz. containing 40 grains of quinine should be used, so as to saturate the whole wall. In some cases the temperature falls finally, all the symptoms disappear and weight is rapidly gained after a single injection, as happened in eight cases. More frequently the effect is only temporary, and it is then advisable to repeat the little operation after about a week, when less pus is commonly obtained. A third injection is not rarely required, but in large abscesses even more, perhaps even four or five, may be required. I have noticed that if an originally present leucocytosis completely disappears, little or no pus is usually obtained at a second aspiration, and uninterrupted convalescence ensues. The continued presence of even a slight leucocytosis is generally an indication for repeating the aspiration. In the common fibrous-walled single abscess no cinchonism results, even from the injection of as much as sixty grains of quinine, but in more acute ones the drug may be absorbed to some extent into the circulation.

**ROGERS'S FLEXIBLE SHEATHED TROCAR FOR STERILE SIPHON DRAINAGE AND QUININE IRRIGATION**

With a special apparatus Rogers drains aseptically the cavity of the abscess and washes it out with sterile quinine solution to kill the amœbæ.

**OPEN OPERATIONS WITH DRAINAGE**

There are various ways of approaching the liver with a view of performing a simply oncotomy. In the main they are divided into two types: the transpleural route and the abdominal route. Some surgeons prefer to explore the liver to determine the presence and location of the abscess before proceeding to operate; others expose the liver and use the needle to locate or determine the presence of an abscess.

*Transpleural route.*—Several surgeons describe various techniques of the transpleural route; all have their advantages and objectionable points. McDill(16) describes a technic in which pneumothorax is obviated. Essentially it is as follow: A curvilinear incision to expose the right ninth and tenth ribs is made in the midaxillary line. All the tissues down to, but not including, the fascia overlying the muscles are reflected in one flap. The periosteum of the exposed ninth rib is dissected out and 10 centimeters of it is resected. The resulting gutter is closed with a running catgut suture through the entire thickness of the musculature. Just above the tenth rib an incision is made through all layers of the chest wall and the diaphragm. While this incision is accomplished, the fingers of an assistant firmly press the loosened chest wall inward and against the diaphragm to prevent

pneumothorax when the incision opens or crosses the pleural sac. The diaphragm and the chest wall are finally sutured and the liver explored with a needle. If abscess is found, it is either incised or left alone for forty-eight hours, allowing parietovisceral adhesions to form, before incision is made. A short rubber tube is used for drainage.

*Abdominal route.*—While all the operations of this type are essentially the same in principle, there are important differences in the technic either for attaining better asepsis or better drainage.

The principle of Manson's method is briefly as follows: A trocar and cannula 9 millimeters in diameter and 10 centimeters long is used. Through this a rubber drainage tube stretched by a long stilette, the extremities of which are placed in buttons tied into the ends of the tubing, is introduced. The trocar and cannula are thrust into the liver, and the tubing is stretched by the stilette introduced inside the cannula after removal of the trocar. The cannula and the stilette are then removed, allowing the rubber tubing to contract and fit snugly into the punctured wound in the liver, thus preventing the escape of pus and thereby contaminating the serous sac and at the same time lessening the chances of hemorrhage. Cantlie<sup>(34)</sup> reports 82 per cent recoveries in 100 cases by operation of this method.

Rhoads,<sup>(35)</sup> realizing the possible dangers associated with aspiration as a method of locating the abscess, and the uncertainty of obtaining reliable information, advocates direct palpation of the liver through a high, right rectus incision in every suspected case, as a more satisfactory method for locating the pus collection. If the abscess is located in the lower part of the right lobe, lobus Spigelii, lobus quadratus, or the left lobe, evacuation is accomplished as follows according to the words of the author:

The assistant being ready with gauze sponges clamped to carriers, an incision 4 cm. in length and 1 cm. or more in depth is made through the capsule. If this has not reached the pus, a closed broad-ligament clamp is pushed through the opening, past the fibrous boundary of the abscess and into the cavity, opened so that the blades are separated at least the length of the surface cut, and withdrawn. The fibrous wall is very dense in some cases, varying from .5 cm. to 2 cm. in thickness, according to the age of the abscess, and may require considerable force to overcome its resistance as the clamp is pushed through. As the thick, brownish-yellow pus appears along the path of the instrument, the assistant sponges it away rapidly from the opening, as little of the material as possible being permitted to flow over the gauze protecting the intestines. The clamp is inserted on successive times as the flow lessens until the cavity has emptied itself, and its

interior is then examined with the finger. If trabeculae divide the cavity into various compartments, they are broken down, and loose shreds of necrotic tissue hanging from the shaggy wall are brought away. The interior is wiped dry with narrow strips of gauze armed on a clamp, several of the strips being allowed to remain in the cavity after it is comparatively cleansed, and the free ends are brought to the surface of the abdomen to act as a drain. Alongside these strips is inserted a large, firm, rubber tube, 1.5 cm. in diameter, with 2 openings cut into its sides near the end projecting into the abscess cavity, and the free end is anchored in the abdominal incision at the point best adapted for drainage. The soiled gauze strips protecting the intestines are removed after clean strips in equal number have been placed underneath them, i. e., between the original gauze strips and intestines, and these in turn are substituted by one strip, 10 cm. wide, for abdominal drainage, carried to the farthest point posteriorly underneath the liver, and so placed that when spread out its edges will overlap the liver incision. If the operation was on the upper anterior surface of the liver the gauze protecting the suprahepatic space is removed, the space is wiped dry, and narrow gauze strips 4 cm. wide are placed on each side of the liver cut and brought out of the abdominal wound. We have then these gauze strips for drainage through the abdominal wall, beside the rubber tube; 1 piece 10 cm. wide, and of 8 thicknesses, for the abdomen; 2 narrow strips for the abscess cavity (2 narrow strips being used in preference to 1 broader one on account of ease in withdrawal); and if the abscess was on the upper anterior surface, 2 additional narrow strips as guards of the suprahepatic space, 1 on either side of the liver cut. The destination of each set of strips is marked by tying black or white sterile silk to the free ends before the abdomen is closed.

Dr. P. K. Gilman, of the department of surgery, University of the Philippines, in his wide experience with amoebic hepatic abscess has evolved a very good operation. In this method the high, right rectus incision is utilized and a thorough digital examination of the liver is made. In certain cases where this method fails, a narrow gauze packing such as that used in uterine operations is tucked in around a circumscribed area of the liver, walling off the abdominal cavity. A long aspirating needle attached to a glass syringe is thrust, in various directions, into the liver substance. Once the abscess cavity is discovered, the needle is withdrawn and a large Ochsner's gall bladder trocar attached to a long rubber tubing is pushed into the abscess cavity. As a rule the thick viscid liver pus flows out freely, but if the flow is sluggish, a large syringe may be used to suck the pus out. With a little pressure exerted upon the abdomen to cause the intestines to push up against the inferior surface of the liver, the abscess cavity may be completely evacuated; however, complete evacuation is not necessary. Immediately after withdrawing the trocar, one end of a piece of rubber tubing, slightly larger than the trocar and 60 to 70 centimeters long, is introduced into

the abscess cavity by means of an artery clamp. Pieces of one-inch iodoform gauze are placed on the liver surface immediately around the rubber tube and covered by the lips of the incision when the latter is finally sutured. After removing the packing used for walling off the other viscera, the incision is closed in layers, anchoring the tube to the edges of the incision with silkworm gut sutures. To the ends of the iodoform gauze safety pins are fastened to prevent the chance of losing them. When the patient is returned to his bed, the distal end of the rubber tube is placed in a large white bottle suspended from the middle portion of the right side of the bed.

This method has two very good features which make it the operation of choice. These are the use of Ochsner's gall bladder trocar, which obviates the chances of contaminating the peritoneal cavity by the avoidance of the overflow of pus in the operative field, and the postoperative drainage by means of the long rubber tubing. With our cases we have observed that during operation the abscess cavity does not contract very much, a fact which is especially true with old abscesses with relatively thick walls. However, during the three or four days following operation, much contraction takes place. In some cases this was apparent from the accumulation of as much as a liter or more of pus in the drainage bottle during the first twelve hours following operation. As the pus passes through the tube easily, we derive another advantage of keeping the operative wound and the dressings perfectly clean.

#### POSTOPERATIVE TREATMENT

In the open operations described above all the drainage tubes provided are just long enough to protrude out of the incision. Fairly thick dressing is applied over the wound. This is changed as often as demanded by the amount of discharge. If the tube is acting properly, it is not disturbed during the first week. Later it may be removed and cleaned, and as the discharge diminishes in amount, it may be gradually shortened. In the majority of our cases the abscess cavity was not irrigated with any kind of solution, while in a few others in which the discharge showed amoebæ quinine in 1 to 1,000 solution and fluid extract of ipecacuanha in a solution of 1 to 500 were used. In cases with intercurrent intestinal amoebiasis, emetine given intravenously, 1 grain daily, and ipecacuanha, in salol-coated pills, were administered. The value of emetine hydrochloride in extremely ill cases cannot be overestimated, for we have saved many such

by administration of this drug. The after treatment in cases operated upon by Gilman's method is essentially the same. After one week the tube is cut near the operative incision and covered with dressings.

#### CONCLUSIONS

1. Seventy-nine per cent of liver abscess cases among Filipinos as seen at the Philippine General Hospital are distinctly associated with intestinal amoebiasis.
2. Liver abscess is relatively frequent among Filipinos.
3. There is apparent predominance of cases of liver abscess among Filipinos during the cool and rainy months.
4. The age incidence corresponds with that of other countries.
5. Filipino women are not as immune to the disease as European or American women.
6. Occupation plays an important rôle in the etiology of liver abscess, as in certain occupations the individuals are brought to a condition or position favorable to infection.
7. The right lobe is the most frequent site of the abscess in our cases among Filipinos.
8. Fever is not typical in cases of amoebic abscess of the liver.
9. There is nothing characteristic in the pain symptoms.
10. The blood picture varies—being normal in many cases. In the majority of the cases, the polynuclear count is normal. There is no eosinophilia in our cases, nor is there any increase in the mononuclears.
11. Diagnosis is easy in advanced cases, but extremely difficult in early cases with small abscesses.
12. Intestinal hemorrhage as a complication of liver abscess is not necessarily fatal.
13. Mortality among Filipino cases is relatively low, in spite of the fact that they come very late for treatment.

In conclusion, I desire to express my gratitude to Drs. W. E. Musgrave, P. K. Gilman, and B. C. Crowell and the Misses Esperanza Concepcion, Carmen Ocampo, and Catalina Gallaron, for many favors and valuable assistance.

#### REFERENCES

- (1) MANSON. *Tropical Diseases*. William Wood and Co., New York (1910).
- (2) CASTELLANI and CHALMERS. *Manual of Tropical Medicine*. Baillière, Tindall and Cox, London. 2d ed. (1913).
- (3) SAUNDBY and MILLER. *Brit. Med. Journ.* (1909), 1, 771.

- (4) DAVIDSON. A System of Medicine. By many authors. Albutt, T. C., and Rolleston, H. D. Macmillan and Co., London (1907), 2, pt. 2.
- (5) CORLETTE. Amœbic dysentery and abscess of liver: An indigenous New South Wales case. *Med. Journ. Australia* (1915), 1, 427.
- (6) FUTCHER. A study of cases of amœbic dysentery occurring at the Johns Hopkins Hospital. *Journ. Am. Med. Assoc.* (1903), 41, 480.
- (7) TUTTLE. Cited by Anders and Rodman. The treatment of amœbic dysentery, specially by appendicostomy. *Journ. Am. Med. Assoc.* (1910), 54, 503.
- (8) BOGGS. Amœbic dysentery in the Southern States. *Virginia Med. Semi-monthly* (1908), 13, 9.
- (9) MUSGRAVE. Amœbiasis: Its association with other diseases, its complications and its after effects. *Phil. Journ. Sci.* (1906), 1, 547.
- (10) FERNANDEZ. Contribucion al diagnostico radiologico y al tratamiento medico quirurgico de los accesos del higado. *Actas, Memorias y Comunicaciones de la Segunda Asamblea Regional de Medicos y Farmaceuticos de Filipinas*, Manila (1914).
- (11) CROWELL. The chief intestinal lesions encountered in 1,000 consecutive autopsies in Manila. *Phil. Journ. Sci., Sec. B* (1914), 9, 453.
- (12) GILMAN. A report of the first one hundred autopsies at the Philippine Medical School. *Ibid.* (1908), 3, 211.
- (13) Cited by Davidson. No. 4.
- (14) STRONG. *U. S. Army Med. Rep.* Washington, D. C. (1900).
- (15) ROBINSON. Tropical abscess of the liver. *Trans. Nat. Assoc. U. S. Pension Exam. Surg.*, Rochester, N. Y. (1908), 1, 161.
- (16) McDILL. Tropical infections of the derivatives of the primitive gut; their complication and treatment. *Surg., Gyn. and Obstet.* (1911), 13, 523.
- (17) Cited by Musgrave. No. 9.
- (18) CRAIG. The etiology and pathology of amœbic infection of the intestine and liver. International clinics. J. B. Lippincott Com., Philadelphia and London (1905), 4 (XIV), 242.
- (19) Cited by Craig. No. 18.
- (20) Cited by Manson. No. 1.
- (21) MUSGRAVE. Symptoms, diagnosis and prognosis of uncomplicated intestinal amœbiasis in the tropics. *Journ. Am. Med. Assoc.* (1905), 45, 830.
- (22) ROGERS. Fevers in the Tropics (1910).
- (23) WOOLLEY and MUSGRAVE. The pathology of intestinal amœbiasis. *Bull. P. I. Gov. Labs.* (1915), No. 32.
- (24) Cited by Woolley and Musgrave. No. 23.
- (25) COFFIN. Tropical liver abscess. Report of three cases with special reference to blood findings. *Am. Med.* (1906), 11, 134.
- (26) McDILL. Dysenteric abscess of the liver in the Philippine Islands. *Journ. Am. Med. Assoc.* (1907), 49, 491.
- (27) ROGERS. Amœbic colitis in India: Prevalence, diagnosis and emetine cure. *Lancet* (1912), 2, 1062.
- (28) DEEKS and SHAW. Amœbic colitis (amebic dysentery). *New Orleans Med. & Surg. Journ.* (1911), 64, 1.
- (29) CHALMERS and ARCHIBALD. The cure of amœbic dysentery. *Journ. Trop. Med. & Hyg.* (1915), 18, 181.
- (30) OSLER. Cited by McDill. No. 16.

- (81) DUDLEY. Abscess of the liver rupturing into the lesser cavity of the peritoneum and giving rise to peculiar symptoms. *Journ. Am. Med. Assoc.* (1907), **49**, 39.
- (82) CYR. Quoted by Davidson. No. 4.
- (83) STRONG. Intestinal hemorrhage as a fatal complication in amœbic dysentery and its association with liver abscess. *Bull. P. I. Gov. Labs.* (1905), No. 32.
- (84) Cited by Rogers. No. 22.
- (85) RHOADS. Treatment of abscess of the liver. *Am. Med.* (1903), **6**, 659.



## TWO CASES OF BALANTIDIAL COLITIS

By C. H. MANLOVE

(From the Department of Pathology, College of Medicine and Surgery,  
University of the Philippines)

The disease in man produced by *Balantidium coli* with a fatal termination can scarcely be called a common one in the Philippines, although, according to Walker,(4) "the presence of *Balantidium coli* in man in the Philippines is rather common."

An estimate of the occurrence of the disease in the Philippines may be taken from the following: Strong<sup>(3)</sup> recorded 1 death in 1904; Bowman<sup>(1)</sup> recorded 2 deaths up to 1911; Willets<sup>(5)</sup> recorded 2 cases in one of the provinces without a death; Walker<sup>(4)</sup> found 35 cases on the records at Bilibid Prison up to 1913, and he found 8 new cases in 1913; in the Philippine General Hospital there are 20 cases on record, including the 2 cases I wish to report. The number of deaths recorded in the Philippines is 5 from a total of 66 cases.

Strong, in 1904, reported a general review of 127 cases which he collected from the literature, including a case of his own. He found that of the 35 deaths recorded there were 32 autopsies performed, of which 28 showed an ulcerative colitis and 3 a chronic catarrhal colitis.

Walker worked on experimental balantidiasis, for which he infected monkeys with *Balantidium coli* derived from human beings and from pigs. Some of his conclusions are as follows:

Parasitization of man with *Balantidium coli* is relatively common in the Philippine Islands. \* \* \*

A large proportion of the pigs in and about Manila are parasitized with balantidia. \* \* \*

Morphologically *Balantidium coli suis* is identical with *Balantidium coli hominis*. \* \* \*

The early lesions of the intestine of monkeys infected with *Balantidium coli* consist only of a slight hyperæmia with or without punctiform haemorrhages.

Histological examination of the tissues of monkeys recently infected with *Balantidium coli* shows changes, notably vascular dilation, minute haemorrhages, round-cell infiltration and eosinophilia, which distinguish them from lesions of bacterial origin.

*Balantidium coli* was never found entering the tissues through the lesions in 10 parasitized monkeys having a colitis or ulcerations due to bacteria or other causes.

In those monkeys in which infection took place, the balantidia entered the tissues through the sound intestinal epithelium.

*Balantidium coli* can produce bacteriologically sterile abscesses in the submucosa of an infected intestine.

*Balantidium coli* is the primary etiologic factor in the symptoms and lesions of balantidial dysentery.

The latency prevalent in balantidiasis of man is due chiefly to the fact that the patient, although parasitized, is not infected with *Balantidium coli*, but in part to the chronicity of the ulcerative process in infected cases.

Walker, in examination of the intestines in the early stages of the infection, found the epithelium intact except for a mechanical injury, which he attributed to entrance of the balantidia or to minute hemorrhages, but there was no exudate or ulceration. He found more or less congestion of the blood vessels, and the tissue infiltration, which was slight, was of round cells and eosinophiles. Those sections of the colon which did not show balantidia showed either a catarrhal or diphtheritic exudate or ulceration, usually associated with polymorphonuclear infiltration of the mucosa and submucosa.

The histological report of Strong is similar to that of Solowjew, which is as follows:

The parasites were found invading the mucosa, submucosa and muscular layers. They were less numerous in the areas which showed marked necrosis and were found in the margins of more healthy tissue which surrounded these areas. The capillaries of the mucosa and submucosa were dilated, contained parasites and often showed hemorrhage about them. Often the amount of infiltration was small about single parasites in the tissues. However, when the parasites were found in large numbers the infiltration was very marked. The ulcerations extended in places down to the muscular coat, and their edges were usually undermined. The lymph glands were hypertrophied and hyperemic. No parasites were found in any other organ than the large intestine. In the mesenteric glands, spleen, liver, and kidneys there was considerable pigment inside the leukocytes in the blood vessels. No tubercle bacilli were found in the sections.

#### CASE REPORTS

##### CASE I

*History.*—The first case to be reported is one of a Filipino male, age 16, who was admitted to the Philippine General Hospital on March 1, 1916, at 3.30 in the afternoon, complaining of bloody diarrhoea, weakness, and loss of weight. Nothing could be determined as to his method of living or concerning the family and past history beyond the fact that he attended school.

The first intestinal symptoms began about two months previous to admission to hospital with frequent bloody bowel move-

ments, which stopped after several days without treatment. Following this attack he had some irregularity of defecation with alternation of diarrhoea and constipation. During the month previous to admission there was a daily chill and fever, which continued until the present attack.

The present attack began about February 22, 1916, nine days before admission, with frequent bloody bowel movements which occurred almost every fifteen minutes. During this attack there was a moderate grade of fever, abdominal pain, and malaise.

He was treated at first for amœbic dysentery, and in an examination of the faeces, which was made before his admission to the Philippine General Hospital, no pathogenic organism was found. After his admission, before a laboratory examination had been made, a tentative diagnosis of bacillary dysentery, pulmonary tuberculosis, and malaria was made.

A summary of the physical findings is as follows:

The patient was restless, weak, and very much emaciated.

The pulse was small, weak, and rapid, and it fluctuated between 85 and 120, with an average of about 110 per minute.

The temperature varied between 36° and 38.5° C. It was generally subnormal in the early morning and might gradually or suddenly rise, sometimes varying as much as 3° C. in two hours.

The respiratory system showed areas of dullness and some crepitant râles over the apices. The respiratory rate averaged thirty per minute.

The nervous system was apparently normal, though the patient was dull and apathetic.

There was a more or less continuous diarrhoea throughout the course of the disease.

*General course of treatment.*—Throughout the eight days the patient was in the hospital, a continual proctoclysis of normal salt solution by the drop method was used. Proctoclysis of adrenalin chloride, 25 drops to 1 liter of salt solution, was also used. Quinine enemas of varying strength were used daily. On the second and third days after admission he received 30 cubic centimeters of normal horse serum intramuscularly, which produced a very appreciable effect in decreasing the amount of blood in the faeces.

*Laboratory reports.*—The number of bowel movements while in the hospital was 24, of which 15 occurred during the first three days. The faeces were thin, watery, blood-colored, and contained at all times large numbers of *Balantidium coli*, blood cells, mucus, and ova of *Trichuris*.

The urine was alkaline in reaction and free from sugar and contained a decided trace of albumin and abundant amorphous phosphates.

The blood was negative for typhoid and malaria. The haemoglobin was 75 per cent. The leukocytes on March 2 numbered 8,400, while on March 3 they numbered 15,400, with a differential count as follows:

Polymorphonuclears, 85 per cent; small lymphocytes, 10 per cent; large lymphocytes, 1 per cent; transitionals, 2 per cent; and large mononuclears, 2 per cent.

The autopsy was performed March 9, 1916, at 9 o'clock in the morning, two and one-half hours after death. The faeces were examined at this time, and numerous motile *Balantidium coli* were found. The anatomic diagnosis was as follows: Acute and chronic ulcerative colitis (balantidial), intestinal hemorrhage, acute suppurative pleuritis, bronchopneumonia, acute parenchymatous nephritis, acute dilatation of the right ventricle of the heart, hyperplasia of spleen, trichuriasis.

The body is that of a very poorly nourished adult Filipino male, age 16 years, weighing 25.02 kilograms and having a length of 147 centimeters. The skin is pale brown and apparently normal. The eyes are sunken, and the cornea are turbid. The hair is black, straight, and coarse and is limited to the pubes and scalp. The teeth are in fairly good condition. The superficial lymphatic glands are not palpable. Rigor mortis is present throughout the body, and suggillation is present in the dependent parts of the body.

On section the subcutaneous fat is almost completely absent, and the muscle has a brownish red color and is rather dry.

The abdomen. The serosa of the entire intestinal tract has a dark grayish color and is somewhat moist. The diaphragm is located at the fifth rib on the right and at the fifth interspace on the left. The abdominal viscera lie in normal relationship to each other. The omentum is free from fat.

The thorax. The thymus is very small, pale, and soft. On the right pleura are some fibrous adhesions posteriorly, but otherwise it is smooth and moist, and the sac contains no free fluid. The left pleural sac contains about 200 cubic centimeters of thin, creamy, and flocculent puslike material, which forms a thin coating over the lower lobe of the lung.

The lungs weigh 447 grams and float high in water, with the exception of the lower lobes, which are partially submerged. The upper lobes of both lungs crepitate throughout. The lower lobe of the left lung shows a large, consoli-

dated area covering from 5 to 8 centimeters of lung tissue, which upon section shows a smooth grayish to brown surface with reddish brown, compact, raised, airless areas from which a very small amount of fluid exudes on pressure and which measure from 1 to 2 centimeters in diameter. The lower lobe of the right lung shows areas similar to those of the lower lobe of the left lung and also one large consolidated area of 4 to 5 centimeters in diameter. Many of these areas are abruptly outlined with apparently normal lung tissue. On section of the upper lobes they present a surface which is pale, smooth, air-containing, and apparently normal. The bronchi contain a thin mucoid material, and the mucosa shows no appreciable changes.

The heart. The parietal pericardium is pale gray, smooth, and thin. The pericardial sac is apparently normal. The epicardium is pale and smooth, though some of the coronary vessels have a tortuous appearance. The heart itself weighs 147 grams and is normal in shape. The auricles are filled with blood. The tricuspid ring almost admits four fingers, and the right ventricular cavity is enlarged and its walls are very thin. The mitral ring admits two fingers, and the ventricular cavity appears to be enlarged and the walls slightly thinner than normal. The muscle is dark brown and is very moist and rather firm. The blood is coagulated, forming coagula of chicken-fat consistency.

The spleen weighs 330 grams. It is firm and about normal in shape, and the capsule is pale gray. It cuts readily, showing a smooth, very compact dark brown surface, which is not very moist, and upon the surface the strands of interstitial tissue are visible.

The adrenals weigh 12 grams and are apparently normal.

The kidneys weigh 192 grams. They are about normal in shape and consistence. They cut easily, and the cut surface bulges. Upon the cut surface the pyramids are about normal in size, compact, and pale with reddened outline, while the cortex is pale with red linear marking. The capsule strips very easily, exposing a pale surface marked with numerous stellate injections.

The contents of the *small intestine* vary from a thick, creamy yellowish brown material in the jejunum to a thick blackish fluid in the lower ileum. The contents of the colon vary from a thick black fluid in the ascending and transverse colon to a soft, semisolid, thick, turbid black fluid in the descending colon. Trichurides are present.

The walls of the *colon* are somewhat thickened and are

not friable. The mucosa is more or less ulcerated throughout its entire length. In the rectum and adjoining 5 to 10 centimeters of the descending colon it shows the most ulceration, and here the mucosa is reddened, thickened, and riddled with ulcers. In the cæcum it shows almost as numerous ulcers, but here they are more extensive than in the rectum. In the transverse colon and other parts of the colon the ulcers are scattered more widely apart.

The ulcers may be divided into three stages according to the degree of involvement of the colon wall: an early, medium, and late. All three stages are found throughout the entire colon, but predominate as follows: Those in the cæcum are mostly in a late stage with some early and medium found here and there; those of the rectum are mostly of the medium stage with the late stage next in frequency; those of the transverse colon are of all three stages, of which the medium predominates, with one very large late ulcer measuring 4 to 5 centimeters in diameter, which has very irregular, undermined, reddened edges, with a flat base upon which the muscle is visible. The early ulcer is evidenced by a slight, firm elevation of the mucosa, which is reddened and shows a pale central depressed area, which measures from pin point to 1 or 2 millimeters. The medium ulcer is evidenced by a distinct, slightly raised, hemispherical area with a depressed, necrotic center, which measures from 1 millimeter to 1 centimeter. The edges are puckered, irregular, undermined, and deeply reddened and have a reddened areola of mucosa about them. The bases are pale and necrotic, appear flat, and are located in the submucosa. The late ulcers average about 2.5 centimeters in diameter. They are very irregular in shape, with edges that are not elevated but are deeply undermined. The bases are flat and smooth, are located on the muscular coat, and are covered with necrotic material.

The mucosa of the *small intestine* is pale, smooth, and moist and is apparently normal.

The *stomach* is normal.

The *pancreas* is pale and firm, but shows no other changes.

The *mesentery* is practically free from fat, and the lymphatic glands are very pale, but apparently normal.

The *liver* weighs 1,285 grams. It retains its shape after removal and is slightly firmer than normal. The capsule is smooth, glistening, and bluish brown. The liver cuts easily, showing a smooth dark brown surface which is rather moist; the lobules are not distinct. The bile ducts and vessels are apparently normal.

The *gall bladder* contains a very thick, viscid black bile, while the mucosa and walls are apparently normal.

The *urinary bladder* contains a small amount of amber-colored urine, and the mucosa is apparently normal.

Histologically the colon presents changes which vary from a simple catarrh to extensive ulceration involving the muscular coat.

*Changes in the mucosa.*—The mucosa of all parts examined has undergone more or less catarrhal inflammation, and in places it is covered with a superficial pseudomembrane of hemorrhagic and necrotic material. The capillaries are dilated, and many of them are ruptured.

Here and there may be seen distinct ulcers of 1 to 2 millimeters in diameter whose base is superficial to the muscularis mucosæ. There are also areas of 2 to 3 millimeters in diameter where the superficial epithelium has desquamated, while the epithelium at the base of the glands and the interglandular papillæ remain. The papillæ are necrotic near the surface, but in the deeper parts they are thickened, fibrous, and oedematous and are infiltrated with plasma cells and lymphocytes. The blood vessels in the superficial parts of the papillæ are widely dilated and ruptured and communicate with the surface, which is covered with a pseudomembrane containing balantidia.

Where the mucosa forms the margins of the ulcers, there is formation of goblet cells, desquamation of epithelium, necrosis, and infiltration of plasma cells, of round cells, and of some polymorphonuclear neutrophile leucocytes. The blood vessels are dilated, ruptured, and partially or completely obliterated with fibrin thrombi, and in many instances they communicate with vessels in the submucosa showing similar changes.

The balantidia in relation to the mucosa are found on the surface, in the tubules of the glands, within the glandular walls, in apposition to the muscularis mucosa, just penetrating the glandular basement membrane, in the superficial ulcers, and in the solitary lymphoid follicles. They are found both in direct relation to ulcers and in mucosa which is not in close contact with ulcers. In no instance is there any definite cellular reaction surrounding a singly located organism.

*Changes in the submucosa.*—The ulceration in places extends to the submucosa, in which the change varies in degree from a superficial involvement to one extending to the muscle. The ulcers have overhanging, undermined edges which curl into them. They are deeper at their lateral extremities, leaving a raised necrotic base whose apex in some instances is level with the sur-

rounding mucosa, giving the ulcer an inverted bowl shape and leaving considerable submucosa in apposition to the undermined mucosa. Surrounding the ulcers the submucosa is oedematous, thickened, and more or less infiltrated with round cells and polymorphonuclear neutrophiles in groups and more scattered. The infiltration is closely limited to the ulcer and is least in evidence beneath the intact mucosa beyond the margins. The margins of the ulcer are densely infiltrated and show considerable necrosis. Here the blood vessels are widely dilated, some being ruptured and many partially or completely obliterated with fibrin thrombi.

The openings of the ulcers through the mucosa vary from wide openings of 1 to 2 centimeters to fistulous openings of 1 to 2 millimeters in diameter, and these communicate with large cavities in the submucosa which are filled with balantidia and necrotic material. Some of the superficial ulcers involve the solitary lymphoid follicles. Balantidia are found scattered through these follicles, and also there may be groups of twenty or more balantidia found in the lateral deep margins of the ulcers.

The balantidia invading the deeper part of the submucosa are found at the lateral extremities of the ulcers in groups of fifty to a hundred, where there is usually much necrotic material about them and much peripheral cellular infiltration. Scattered through the base and intermingled with the necrotic contents of the ulcer, they are in small numbers and usually singly. They are also present in the tissues about the ulcers, singly and in groups, where they are surrounded by a dense cellular infiltration. They may be seen within the blood vessels of the margins and bases and elsewhere in the submucosa in close relation to the ulcers. The balantidia occur in large and small groups where the submucosa is intact about them, although in this case they are in close relation to an ulcer or the mucosa over them shows inflammatory changes. Here there may be much or little cellular infiltration about them. Those found in vessels or singly are not surrounded by any cellular infiltration, while those in groups are surrounded by more or less cellular infiltration.

*Changes in the muscle.*—The muscle is involved by, and forms the base for, the most extensive ulcers, at which places it is infiltrated with plasma cells, round cells, and polymorphonuclear neutrophiles in groups and scattered and shows some necrosis. The blood vessels about the involved areas are widely dilated and surrounded by cellular infiltration. The subserous tissue

in apposition to the ulcers is œdematosus and slightly infiltrated, while the serosa opposite the extensive ulcers is covered with a fibrinohemorrhagic material, which shows some cellular infiltration.

Balantidia are found within blood vessels of the muscle, also in the subserous tissue, where they are both within blood vessels and lying free. They are found in varying numbers in the necrotic material covering the bases of the ulcers, where there is cellular infiltration about them, while the organisms found in the muscle and subserous tissue are free from any surrounding cellular infiltration.

*Summary of first case.*—A 16-year-old Filipino was in hospital for seven and a half days before death. He had bloody diarrhoea for a few days two months before death, followed by intermittent diarrhoea and constipation. There was a daily chill and fever during the last month. For sixteen days before death there were frequent bloody diarrhoea, moderate fever, abdominal pain, and malaise. Physical examination one week before death revealed emaciation, weakness, slight tachycardia, changes in temperature varying from 36° to 38.5° C., albuminuria, and slight leucocytosis. The faeces were thin, watery, and blood-stained and contained at all times large numbers of balantidia, blood cells, mucus, and ova of *Trichuris*. Autopsy revealed a colitis with bronchopneumonia and degenerative lesions of the viscera.

#### CASE II

*History.*—The second case was a Filipina, age 51 years, who was first admitted to the hospital August 23, 1916, and a diagnosis was made of mixed tumor of the parotid and epithelioma of the cheek. She was discharged September 1, 1916, as incurable. At this time there was no record of intestinal trouble. The patient was again admitted to the hospital September 21, 1916, complaining that one week previously she had become too weak to walk. She was very poorly nourished, with little or no appetite, and was constipated. On the forehead were three small superficial lacerated wounds. On the left side of the neck just below the ear was an irregular swelling with a sinus about 1 centimeter in diameter discharging a moderate amount of pus. The left corner of the mouth was indurated, and this induration was continuous with an induration and ulceration on the inner surface of the cheek, the tongue, and the gums in the region of the lower molars. On the right forearm just above the wrist was an ulcer at the base of which the ulna was exposed. On the buttocks there were numerous scars and one ulcer with

undermined edges. During the ten days after admission, from September 21 until October 1, the bowels remained constipated, and there was no change in the general condition, although the external wounds had healed. However, from October 1 to October 4 there was slight diarrhoea, and from October 4 to October 13 there was an alternation of constipation and slight diarrhoea. During this time the bowels would be constipated for one or two days without any evacuation, which would be followed by several evacuations the next day. She became progressively weaker and died October 13, 1916.

The temperature during the twenty-four days in the hospital remained subnormal, varying from 35.5° to 36.5° C. On two occasions it rose to 38° C. within four hours and as rapidly became subnormal. The pulse fluctuated between 80 and 90 per minute.

The respiration averaged 20 per minute. The number of stools varied from one to three a day with nine days without any passage of stools.

*Laboratory reports.*—The faeces on September 27, 1916, showed *Balantidium coli*, encysted amoebae, ova of *Trichuris* and *Ascaris*, blood, and pus. On October 4 they showed numerous motile *Balantidium coli* and some *Blastocystis hominis*. On October 8 there were no balantidia. The urine showed a decided trace of albumin, some pus and red blood cells, granular casts, epithelial cells, and mucus. The blood was not examined.

The clinical diagnosis was: Epithelioma of mouth, involving cheek, tongue, and upper jaw, mixed tumor of parotid, balantidiasis, trichuriasis, ascariasis, amoebiasis (intestinal), blastocystiasis, and inanition.

The autopsy was performed October 14, 1916, fourteen hours after death. An examination of the faeces at this time failed to reveal any balantidia. The anatomic diagnosis was: Chronic catarrhal colitis (possibly balantidial), chronic diffuse nephritis, chronic ulcerative tuberculosis of the lung, infected tumor of parotid, ascariasis, and trichuriasis.

The body is that of a very poorly nourished adult Filipina, whose age is 51 years, weight 25.10 kilograms, and length 157 centimeters. The skin is dark brown and is shrunken over most of the body. On the lateral surface of the right hip there are several open ulcerative lesions about 2 centimeters in diameter. These extend into the subcutaneous tissue. On the right forearms there are ulcerative lesions, which extend into the subcutaneous tissue. The cornea are very turbid, and the eyes are sunken. The mucosa of the mouth is covered with a whitish

necrotic material. Many of the teeth are missing, and those present show extensive caries. At the left posterior angle of the jaw there is a raised mass which measures about 7 centimeters in diameter and is elevated about 3 centimeters above the surrounding tissue. This shows two sinuses, which penetrate into the mass, and from them exudes a thick, creamy, puslike greenish material. The mass involves the region of the left parotid and submaxillary gland. The central part of it is necrotic and is filled with a greenish puslike material, and the cut surface is compact, whitish, and firm. Rigor mortis is present to some extent throughout the body, and suggillation is present in the dependent portions of the body.

On section there is practically no subcutaneous fat. The muscle is light reddish brown and moist.

The *abdomen*. The serosa of the entire intestinal tract, parietes, and stomach is pale, moist, and apparently normal. The diaphragm is normally located. All the abdominal viscera have gravitated somewhat toward the pelvis.

The *thorax*. The thymus is almost completely absent, and fatty tissue has taken its place.

The *pleural sacs*. The left pleural sac contains fibrous adhesions in the apex, and the right pleural sac is free from adhesions. Otherwise both sacs are moist, do not contain free fluid, and appear normal.

The *lungs* weigh 500 grams. They float very high in water and are large, and crepitation is present throughout, except in the apex of the left lung, where there is a consolidated area of about 5 to 6 centimeters in diameter. Section through this lung shows an abscess cavity of 3 to 4 centimeters in diameter, which contains a thick, creamy grayish yellow pus and whose walls are rough and necrotic. The lung tissue immediately about the abscess is compact and whitish and contains caseous material. Section through the lungs elsewhere shows a smooth, moist reddish surface which is air-containing and apparently normal. The pleura covering the lungs is pale gray with black pigmented mottling. The bronchi have a grayish color, and those of the left lung contain some puslike material.

The *heart*. The pericardium and pericardial sac appear normal. The epicardium has a grayish color, and the coronary vessels are tortuous. The heart itself weighs 176 grams. It is rather firmly contracted. The tricuspid ring admits almost three fingers, and the mitral ring admits barely two fingers. The endocardium covering the valves is thickened, firm, and somewhat roughened. This is noticeable at the bases and the edges of the

leaflets. The ventricles and auricles show no appreciable change from normal. The muscle is brown, and its cut surface is smooth, dull, and moist. The blood is coagulated, forming a coagulum of chicken-fat consistence.

The *spleen* weighs 37 grams. It is about normal in shape and somewhat soft in consistence. The capsule is blue. The spleen cuts easily, showing a smooth, moist, compact reddish surface.

The *adrenals* weigh 9 grams. They are rather firm in consistence, dark brown in color, and show no appreciable change.

The *kidneys* weigh 217 grams. The left kidney measures 12.5 centimeters in length by 6 centimeters in width and 3 centimeters in thickness. The right kidney measures 9 centimeters in length, 5 centimeters in width, and 3 centimeters in thickness. Both kidneys are somewhat firm in consistence and about normal in shape. They cut readily, showing a smooth, moist surface, from which a small amount of blood exudes. Upon the surface the pyramids are very large, compact, glistening, and reddish, while the cortex is mottled and light brown and red, although in places the columns of Bertini are pale and bulging. The capsule strips readily, showing a surface which is slightly roughened by depressions of 0.5 centimeter in diameter, and it has numerous stellate injections upon a light brownish background. In places it is firmly adherent to the kidney substance.

The *intestines*. The serosa has been described. The contents of the small intestine are a thin, mucoid yellowish and brown material, while in the colon the contents vary from a thick, semi-fluid brownish material in the ascending and transverse colon to a thick, mucoid grayish material in the descending colon. The mucosa throughout is thickened, swollen, soft, and velvety, and it has a dark grayish color with a reddish tinge in places, although in the descending colon the mucosa is mottled with what appear to be superficial ulcers. These areas measure about 3 or 4 millimeters. The base appears to be located in the mucosa. The mucosa of the small intestine is pale grayish, smooth, and moist and is apparently normal.

The *stomach* contains some thick mucoid material. The mucosa is grayish and smooth.

The *pancreas* is firm in consistence, but normal in size and shape and shows no appreciable change.

The *mesentery* appears normal.

The *liver* weighs 956 grams. It is reddish brown and is about normal in shape and consistence. The capsule is mottled in

places. The liver cuts readily, showing a smooth, moist, glistening surface, which has a reddish brown mottled appearance. The lobules are plainly visible and show a reddish center and a pale periphery. The bile ducts are surrounded in places with considerable fibrous tissue, and they have a yellowish tinge throughout. The common bile duct measures about 1 centimeter in diameter and contains four or five dead ascarides.

The gall bladder was removed intact for bacteriological examination.

Histologically the changes in the colon are confined to the mucosa. The mucosa shows catarrhal inflammation and some desquamation of the superficial epithelium, and the tubules are filled with mucus. The mucosa is frequently folded in such a manner that the shape of an ulcer is produced with undermined edges. These areas are completely lined with epithelium, but may contain faecal material within which balantidia are embedded. The balantidia are found only on the surface of the mucosa, where they are embedded in faecal material. The tumor in the mouth proved to be an epithelioma.

*Summary of second case.*—A 51-year-old Filipina was under observation about seven weeks. She sought hospital treatment on account of epithelioma of the cheek and a mixed parotid tumor. Weakness was a marked symptom. She was constipated until ten days before death, when intermittent attacks of diarrhoea occurred. She was emaciated and had no appetite, and there were subnormal temperature, normal pulse, normal respiration, and albuminuria. The intestinal condition only assumed importance after examination of the faeces and the finding of balantidia. Autopsy showed a colitis as a complication of the other more important disease.

#### DISCUSSION

In the first case I was particularly careful to exclude the possibility of balantidiasis of the left lung and pleural sac. It is of interest to note that cultures made from the pleural sac remained sterile. The histological examination of the lung and pus did not reveal any balantidia. In view of the fact that the sections of colon show balantidia in blood vessels, there must be a continual entrance of balantidia into the general circulation. However, it is rare to find them producing lesions outside of the intestines, although they have been reported in sputum from a case of supposed lung involvement. In my cases the physical findings cannot be said to be distinctive of balantidiasis. The temperature was one of the most variable features, as it fluctuated from

subnormal to above normal. The absence of eosinophilia in both of these cases seems to support the belief that eosinophiles may or may not be found in all intestinal disturbances. Since the balantidia are found penetrating both the mucosa and submucosa without any surrounding cellular infiltration, it may be safely concluded that they are capable of penetrating apparently healthy mucosa. Here they may produce sterile abscesses which may in time become secondarily infected by the rupture of the mucosa covering them and thus form ulcers. Macroscopically the lesions produced by *Balantidium coli* cannot be differentiated from those of *Entamoeba histolytica*. Microscopically the lesions show a similar cellular reaction, but are easily differentiated by finding the organisms. Many of the balantidia examined in the wall of the colon did not show the typical nuclei, but contained numerous small masses of nuclear-staining material, which resemble chromidia formation, while those examined on the surface of the mucosa show the typical nuclear structures.

As suggested by Dr. B. C. Crowell, the question of the essential pathogenicity of balantidia is an important one, and one which cannot yet be considered to be absolutely settled. It is necessary to determine the invasive powers of the balantidia, that is, whether they may or may not of themselves penetrate the intact mucosa, and if so, whether they pass through the epithelial cells or between the cells. Reasoning from analogy with known facts concerning the action of entamoebæ, and from the known tissue changes described in balantidiasis, it seems necessary to believe that these organisms are essentially pathogenic and that their action is in all ways similar to the action of the entamoebæ. Doctor Crowell expressed the theory that it seems reasonable to conclude that some substance (toxin?) originating from the balantidia is able to produce necrosis of the tissues, and the inflammatory phenomena that occur later are the result of the action of the accompanying bacteria. Also that one could imagine that this hypothetical toxic substance from the balantidia produces a cytolysis of the epithelial cells of the mucosa with which they come in contact and so forms a portal of entrance to the deeper tissues for the organisms.

#### SUMMARY

1. Two cases of balantidiasis with clinical histories and autopsy reports have been added to the five previously published autopsy cases from the Philippines.
2. In one case there was a history of dysentery for approximately two months before death; in the other the intestinal

condition was detected only on routine examination and was unimportant from the clinical standpoint.

3. Balantidiasis is relatively unimportant as a cause of death in the Philippines, but may cause considerable morbidity.

4. As in amoebiasis, extensive intestinal lesions in balantidiasis may be present without giving rise to symptoms.

5. The intestinal lesions in balantidiasis vary from a simple catarrh to deep ulceration. They are characterized by abundant organisms in the intestinal wall with some inflammatory manifestation and by a burrowing necrosis of the submucosa, which is similar to the amœbic lesion. All parts of the colon may be involved. An etiologic diagnosis can only be made by finding the protozoa. Eosinophilia in sections of the intestine has not been prominent in these cases, although it has been emphasized by previous authors.

#### REFERENCES

- (1) BOWMAN, F. B. A case of dysentery caused by *Balantidium coli* with coincident filarial infarction of the spleen. *Phil. Journ. Sci., Sec. B* (1911), **6**, 147-152.  
IDEM. Two cases of *Balantidium coli* infection. *Phil. Journ. Sci., Sec. B* (1909), **4**, 417-423.
- (2) SOLOWJEW, N. Das *Balantidium coli* als Erreger chronischer Durchfälle. *Centralbl. f. Bakt. etc., 1. Abt.* (1901), **29**, 821, 849. Cited by Strong (3).
- (3) STRONG, R. P. The clinical and pathological significance of *Balantidium coli*. *Pub. Bur. Govt. Labs., Manila* (1904), No. **26**, 1-77.
- (4) WALKER, ERNEST LINWOOD. Experimental balantidiasis. *Phil. Journ. Sci., Sec. B* (1913), **8**, 333-351.
- (5) WILLETS, D. G. General conditions affecting the public health and diseases prevalent in the Batanes Islands, P. I. *Phil. Journ. Sci., Sec. B* (1913), **8**, 49-58.



## PROCEEDINGS OF THE MANILA MEDICAL SOCIETY

REGULAR MONTHLY MEETING, MARCH 5, 1917

The regular monthly meeting of the Manila Medical Society was held at 8.30 in the evening, March 5, 1917, in the College of Medicine and Surgery. President Winter was in the chair; 19 members and 2 guests were present.

The minutes of the last meeting were read and approved as read.

As there was no further business to come before the society, the president announced the first paper for the evening, namely, by Dr. José Hilario and Mr. L. D. Wharton on the anatomy of *Echinostoma ilocanum*, with clinical report on some recent cases. The paper was followed by an excellent demonstration of the characteristic anatomy of the Echinostoma.

Dr. José Albert then presented an interesting paper on his experience in the diagnosis and treatment of infantile beriberi. He described an acute, a chronic, and a pseudomeningitic form and described the last form in detail.

The president then asked Doctor Arvisu to read the clinical records of the cases of pseudomeningitic beriberi described by Doctor Albert.

Doctor Gibson next gave a demonstration of the Folin methods for the examination of urine. By these methods he was able to demonstrate that the amount of nitrogen, ammonia, and urea in urine could be determined in approximately thirty-five minutes.

It was then moved and seconded that the society adjourn.

H. G. MAUL,  
*Secretary-Treasurer,*  
*Manila Medical Society.*

### SCIENTIFIC PROGRAM

#### ECHINOSTOMA ILOCANUM (GARRISON) : A REPORT OF FIVE CASES AND A CONTRIBUTION TO THE ANATOMY OF THE FLUKE

By Dr. J. S. HILARIO and Mr. LAWRENCE D. WHARTON

Five cases of infection with *Echinostoma ilocanum* are reported in patients at the Philippine General Hospital. All of the infections were in natives of Zambales Province, Luzon. The symptoms presented were anaemia, with occasional headache and

dizziness. The blood picture showed more or less marked decrease of the haemoglobin percentage, moderate diminution in number of red corpuscles, and eosinophilia in some cases. Treatment consisted of 24 capsules of oleoresin of male fern given in doses of 4 capsules every ten minutes. During the previous day the patient was kept on liquid diet without milk as a preparatory measure for the treatment.

Sixteen worms were obtained from two of the cases after treatment. Specimens ranged from 4.03 millimeters to 7.82 millimeters in length and from 0.98 millimeter to 1.6 millimeters in breadth. The cuticular spines were found to be absent in the majority of specimens and were very easily broken off in those specimens where they were present. Only three specimens showed the oral wreath of spines which is characteristic of the genus. In the one specimen on which these spines could be counted they were found to number 39. The arrangement was similar to that described by Odhner. The structure of the internal organs was found to agree very closely with Garrison's description. Measurements of 25 fresh eggs from faeces gave an average of 101.2 microns by 56.4 microns.

This paper will appear in full with illustrations in a future number of the Philippine Journal of Science.

#### THE PSEUDOMENINGITIC FORM OF INFANTILE BERIBERI

By Dr. JOSE ALBERT

In the diagnosis of infantile beriberi it may be rightly said that the medical man continues to be a student as long as he remains in the profession. Fifteen years ago, when beriberi in infants under 1 year of age was still unknown, I wrote in the death certificates of such cases diagnoses of convulsions, heart failure, pneumonia, and peritonitis. In the twelve years since the existence of infantile beriberi as a distinct disease has been confirmed and generally recognized, two clinical forms or types of this important disease are admitted: the chronic aphonic type which lasts for several weeks and in which hoarseness of voice associated with hypertrophy and dilatation of right heart are the predominant symptoms, and the acute, pernicious, cardialgic type, lasting from several hours to two days, and characterized by intense and incessant crying.

During last year, 1916, I had the opportunity to observe

three cases of infantile beriberi entirely distinct from the two types described above. They were characterized by cerebromeningeal symptoms. I have applied the name "pseudomeningitic form" to this type of the disease. As far as I know, this form has never been described in this country.

The three cases I referred to were treated unsuccessfully outside our clinic as cases of meningitis. Their age varies from 5 to 6 months, somewhat older than the ordinary cases. All were entirely breast-fed, and the mothers had symptoms of rudimentary or latent beriberi. Two of the cases had brothers and sisters who died of infantile beriberi, while the third case was the first child of the family.

The most striking symptom in these patients was drooping of the eyelids—ptosis—a paralytic manifestation of the neuromuscular form according to Professor Takasu, of Osaka. Because of the paralysis of the eyelids, the child has a vacant, idiotic expression. He is drowsy most of the time, the eyes looking upward and the head bent slightly backward. Moderate fever was present at the onset in two cases, while absent in the third. One had marked choreic movements of the limbs, which lasted for from three to four weeks, and on admission this patient presented convulsions of the extremities, twitching of the facial muscles, strabismus, the eyes rolling up, slight rigidity of the neck, and fever of  $38.5^{\circ}\text{C}$ . for two days. Lumbar puncture was performed on this patient with negative results. Two gave a history of having hoarseness of voice at the age of two months, which fact suggests that these cerebromeningeal symptoms are manifestations of a second attack of infantile beriberi.

In all these cases X-ray examinations demonstrated the enlargement of the right heart, the characteristic lesion of the disease.

All were treated with extract of tiqui-tiqui with rapid and marvelous effects, as observed in other forms of infantile beriberi.

In view of these observations I feel justified in presenting to your consideration this pseudomeningitic form of infantile beriberi as a new type of the disease distinct from the aphonic and pernicious types. This form of infantile beriberi simulates meningitis in its clinical manifestation; it presents hypertrophy and dilatation of the heart and is observed in infants older than 3 months, and extract of tiqui-tiqui is its specific remedy.

**A DEMONSTRATION OF THE FOLIN METHODS FOR THE ANALYSIS OF  
THE URINE**

By Dr. R. B. GIBSON

The publication by Folin and Denis<sup>1</sup> of a description of practical colorimetric methods for the determination of the several forms of nitrogen in the urine and blood makes a demonstration of these methods timely. The methods, which are based on direct Nesslerization, are easy, rapid, and accurate. With a little practice they may be carried out by the ordinary physician. These methods are at present being taught to the students in physiological chemistry in the College of Medicine and Surgery of the University of the Philippines. Printed directions for the analyses, as demonstrated before the society, will be furnished on application to the department of physiology.

R. B. GIBSON,  
*Editor of the Proceedings,*  
*Manila Medical Society.*

<sup>1</sup> *Journ. Biol. Chem.* (1916), 26, 473-506.

# THE PHILIPPINE JOURNAL OF SCIENCE

## B. TROPICAL MEDICINE

VOL. XII

JULY, 1917

No. 4

### DEGENERATION OF PERIPHERAL NERVES<sup>1</sup>

BY C. MANALANG

(From the Department of Pathology and Bacteriology, College of Medicine and Surgery, University of the Philippines)

#### TWO PLATES

It is customary in the routine work after an autopsy to examine the peripheral nerves of a beriberic or "suspect" for fatty degeneration of the myeline sheath by the Marchi method, after which a final diagnosis is made. Therefore a person who is not aware of the possible presence of degeneration in nonberiberics and who is not in the habit of examining nerves of cases other than beriberics will often be misled in his conclusions. If the degeneration of the peripheral nerves is accompanied by œdema of the subcutaneous tissue with moistness, congestion, and petechiae of the serous surfaces, marked dilatation and hypertrophy of the right ventricle, congestion and œdema of the lungs, congestion of the viscera, and acute duodenitis, then a diagnosis of beriberi is justified. However, it is possible that the above morbid anatomy may be present in cases which are clinically nonberiberic, with the exception of a right-sided hypertrophy. On the other hand, such an important finding as hypertrophy of the right ventricle may be and is often absent in the acute cases of beriberi. œdema is a constant symptom in the course of beriberi, but may be so trivial in the acute pernicious form, in the rudimentary form, and in the late stages of the disease that it becomes unrecognizable at autopsy. A previous attack of typhoid, pneumonia, diphtheria, or any acute infectious disease may leave sufficient degeneration in the heart muscle to cause sudden cardiac dilatation. Acute cardiac dilatation also occurs in pernicious anaemia, chronic interstitial nephritis, and generalized arteriosclerosis. It is in these cases of sudden deaths of which a clinical history is often lacking that the morbid anatomist will be confronted with difficulties, and the mere presence of

<sup>1</sup> Submitted as a thesis for the degree of Doctor of Tropical Medicine.  
Received for publication April, 1917.

fatty degeneration in the myeline sheath does not justify the diagnosis of beriberi.

The object of this work is twofold: namely, to determine the presence of degeneration in the peripheral nerves of morbidities other than beriberi and to emphasize the presence of the degeneration in nonberiberics.

This paper will treat the subject from the viewpoint of morbid anatomy only, without reference to the clinical history or course of each case studied. It is unfortunate that comparatively few cases of frank beriberi came to the morgue during the period of this study, so that only six could be included in this series. No attempt will be made to compute the incidence of degeneration in terms of percentage, due to lack in number in each class of cases studied.

TABLE I.—*Sources from which material is derived.\**

	Cases.
Philippine General Hospital	48
St. Joseph's Hospital	16
San Lazaro Hospital	27
"Outside"	13
Total	104

TABLE II.—*Interval between death and autopsy.*

	Cases.
Under 12 hours	44
12-24 hours	46
24-36 hours	8
36-48 hours	1
Over 48 hours	5
Total	104

TABLE III.—*Age of cases studied.*

	Cases.
Under 1 year	7
1-5 years	10
5-20 years	14
20-50 years	56
Over 50 years	17
Total	104

TABLE IV.—*Classification of cases according to clinical diagnosis.*

Clinical diagnosis.	Cases.
Pulmonary tuberculosis	16
Asiatic cholera	26
Accidents (acute anemias, fractures, etc.)	10
Cardiac dilatation	4
Beriberi	3
Acute ileocolitis	4

\* The Philippine General Hospital supplied surgical and infectious cases. St. Joseph's Hospital supplied tuberculous cases. San Lazaro Hospital supplied contagious cases. "Outside" supplied accidents, medicolegal, and undetermined cases.

TABLE IV.—Classification cases according to clinical diagnosis—Continued.

Clinical diagnosis.	Cases.
Submersion	3
Bronchopneumonia	3
Lobar pneumonia	1
Surgical shock	1
Undetermined	3
Acute nephritis	1
Cystolithiasis	2
Biliary cirrhosis of the liver	1
Uræmia	1
Typhoid	1
Intestinal tuberculosis	2
Tuberculosis of the liver (?). Carcinoma (?)	1
Cerebral hemorrhage	1
Tuberculous meningitis	2
Carcinoma of the neck and viscera	1
Strangulated hernia	1
Ascariasis (cholera?)	1
Pulmonary œdema	1
Carcinoma of the liver	1
Empyæma	1
Pulmonary hemorrhage (tuberculous)	1
Purpura fulminans	1
Atrophy	1
Acute malaria	2
Puerperal infection	2
Noma (cancrum oris)	1
Electrocution	1
Acute suppurative cholecystitis	1
Hemorrhage from gastric ulcer	1
Chronic nephritis and suppurative pyelitis	1
Total	104

## TECHNIC

From 2 to 4 centimeters of the vagus and posterior tibial nerves are laid on a strip of cardboard and treated as follows:

1. Harden in equal parts of Müller's fluid and formaldehyde (10 per cent) for twenty-four hours.
2. Replace by Müller's fluid and keep in it for fifteen days.
3. Wash in running water for from twelve to twenty-four hours.
4. Transfer the tissue for fifteen days to the following solution:

	cc.
Müller's fluid	2
2 per cent osmic acid solution	0.5
Distilled water	0.5

5. Wash in running water for from twelve to twenty-four hours.
6. Dehydrate in graded alcohols, changing the absolute alcohol twice.
7. Clear in oil of origanum, tease under a dissecting microscope, and mount in chloroform balsam.

It is not necessary to place the nerves from one case in separate bottles and label accordingly, because the posterior tibial is always two to three times larger than the vagus nerve.

Surplus tissues after step 3 are placed in 80 per cent alcohol for future staining if necessary.

A record of the gross conditions of all the organs, tissues, and serous surfaces examined was tabulated with the autopsy number, age, number of hours after death the autopsy was performed, nutrition, clinical diagnosis, cause of death, and the findings in the peripheral nerves. This tabulation simplified computation and classification and made apparent the coincidence of degeneration in certain organic lesions. Table V, giving the causes of death, shows the occurrence of degeneration in all the cases studied.

An arbitrary designation of the extent of degeneration was used in the tables, for instance, + + + for marked degeneration, + + for moderate, + for slight, and — for the absence. The accompanying illustrations at the end of this article show these designations clearly. The type and degree of degeneration in the vagus are identical with those of the posterior tibial.

TABLE V.—*Incidence and degree of degeneration in all the cases studied.*

Cases.	Cause of death.	+ + +	+ +	+	—
25	Enteritis (cholera)		7	16	2
14	Pulmonary tuberculosis		5	7	2
10	Accident (violence)		2	4	4
6	Cardiac dilatation (beriberi)		3	3	
4	Bronchopneumonia			1	3
3	Lobar pneumonia		1	2	
2	Ulcerative colitis (amoebic)			2	
3	Acute suppurative peritonitis			2	1
2	Acute malarial infection	1	1		
2	Acute suppurative endometritis			2	
2	Carcinomatosis		1	1	
10	Cardiac dilatation (acute)	1	2	5	2
1	Generalized tuberculosis				1
1	Sarcoma of right kidney			1	
1	Enteritis (typhoid)			1	
1	Pyonephrosis			2	
1	Cirrhosis of the liver			1	
1	Lymphosarcoma of stomach			1	
2	Intestinal obstruction			2	
1	Tuberculous peritonitis			1	
1	Marsasmus (atrophy)			1	
1	Multiple chloroma	1			
1	Membranous colitis			1	
1	Acute vegetative endocarditis	1			
1	Chronic, interstitial and parenchymatous nephritis		1		
1	Hemorrhage from gastric ulcer		1		
1	Suppurative cholecystitis		1		
1	Gangrenous stomatitis			1	
1	Tuberculous meningitis		1		
2	Submersion		1		1
Total			4	29	65
					16

Table V shows that in a mixed autopsy service in Manila 88 out of 104 cases showed microscopically degeneration of the peripheral nerves by the Marchi method. Of these 88 cases the degeneration was slight in 55, moderate in 29, and marked in 4.

TABLE VI.—*Incidence of degeneration and its degree in different ages.*

Cases.	Age limits.	+	++	+	-	Total.	
7	Under 1 year .....			3	2	7	
10	1 to 5 years .....				8	2	10
14	5 to 20 years .....			5	8	1	14
56	20 to 50 years .....	2	17	30	7	56	
17	50 and over .....	2	4	7	4	17	
	Total .....	4	29	55	16	104	

Table VI shows that of the 88 cases of nerve degeneration more than half (49) occurred between the ages of 20 and 50 years, but no age was exempt.

TABLE VII.—*Classification of kidney conditions with the incidence and degree of degeneration.*

Cases.	Condition of kidneys.	+	++	+	-	Total.
41	Acute parenchymatous nephritis and acute parenchymatous degeneration .....	2	13	20	6	41
32	Chronic interstitial nephritis .....	2	11	16	3	32
7	Congestion .....		3	3	1	7
6	Decomposed .....		1	3	1	5
5	Anæmia .....			3	1	5
1	Tuberculosis .....				1	1
5	Normal .....			3	3	6
2	Sarcoma .....			2		2
3	Pyonephrosis .....			3		3
2	Chronic parenchymatous nephritis .....			2		2
	Total .....	4	29	55	16	104

Table VII shows that of the 88 cases of nerve degeneration 69 had nephritis of some form.

TABLE VIII.—*Classification of cases to show condition of nutrition in terms of number of cases and incidence of degeneration.*

Cases.	Poorly nourish-ed.	Fairly well-nourished.	Well nourish-ed.	Total.
Without degeneration (-) .....	5	4	7	16
With slight degeneration (+) .....	13	10	32	55
With moderate degeneration (++) .....	13	1	15	29
With marked degeneration (+++) .....	1		3	4
Total .....	32	16	57	104

TABLE IX.—Cause of death and interval before autopsy in cases with good nutrition and with (+) degeneration.

Cases.	Cause of death.	Hours after death.
3	Acute cardiac dilatation .....	8, 19, 8
1	Ulcerative colitis .....	27
1	Cardiac dilatation with stenosis (mitral) .....	35
2	Acute anaemia .....	22, 7
1	Fractures of pubic and sacral bones .....	24
1	Bronchopneumonia .....	21
1	Lobar pneumonia .....	19
1	Suppurative peritonitis .....	4
1	Pulmonary tuberculosis .....	7
1	Cirrhosis of the liver .....	5
1	Intestinal obstruction .....	3
13	Enteritis (cholera) .....	17, 19, 31, 19, 7, 8, 4, 18, 21, 19, 14, 12, 31
1	Acute anaemia from carotid .....	14
1	Occipitovertebral dislocation .....	(?)
2	Suppurative endometritis .....	3, 15
1	Infantile beriberi .....	5
32		

TABLE X.—Cause of death and interval before autopsy in cases with fair nutrition and with (+) degeneration.

Cases.	Cause of death.	Hours after death.
1	Acute cardiac dilatation .....	3
1	Suppurative peritonitis .....	22
1	Enteritis (typhoid) .....	23
1	Tuberculous pneumonia .....	25
1	Pyonephrosis .....	10.5
1	Intestinal obstruction .....	10
1	Tuberculous peritonitis .....	12
1	Cardiac dilatation with mitral stenosis .....	29
1	Enteritis (cholera) .....	9
1	Lobar pneumonia .....	24
10		

TABLE XI.—Cause of death and interval before autopsy in cases with poor nutrition and with (+) degeneration.

Cases.	Cause of death.	Hours after death.
5	Pulmonary tuberculosis .....	5, 16, 15.5, 9.5, 22
1	Pyonephrosis .....	22.5
1	Sarcoma of right kidney .....	23
1	Primary carcinoma of liver .....	7
1	Lymphosarcoma of intestine .....	12
1	Ulcerative colitis .....	13
2	Enteritis (cholera) .....	5, 9
1	Gangrenous stomatitis .....	3
13		

TABLE XII.—Cause of death and interval before autopsy in cases with poor nutrition with marked and moderate degeneration.

Cases.	Cause of death.	Degener- ation.	Hours after death.
1	Multiple chloroma.....	+++	14
5	Pulmonary tuberculosis .....	+ +	22.5, 16.5, 82(?). 58, ?
1	Lobar pneumonia .....	++	17
1	Beriberi .....	++	19
1	Atrophy .....	+ +	19
1	Acute malaria .....	++	4
1	Suppurative cholecystitis .....	+ +	15
1	Hemorrhage from gastric ulcer .....	++	51
1	Carcinomatosis .....	++	12
1	Chronic interstitial and parenchymatous nephritis.....	++	6
14			

TABLE XIII.—Cause of death and interval before autopsy in well-nourished cases with marked and moderate degeneration.

Cases.	Cause of death.	Degener- ation.	Hours after death.
8	Acute catarrhal enteritis (cholera) .....	++	5, 15, 9.5, 7, 19, 2, 8, 16
2	Acute anæmia from stabs .....	+ +	14, 3
1	Submersion .....	+ +	48
1	Electrocution .....	+ +	16
1	Bacillary dysentery .....	++	15
1	Acute malaria .....	+++	18
1	Cardiac dilatation with arteriosclerosis .....	+++	14.5
1	Tuberculous meningitis .....	++	2
1	Acute beriberi (adult) .....	+ +	10
1	Vegetative endocarditis with arteriosclerosis .....	+ + +	4
1	Infantile beriberi .....	+ +	15
19			

Tables VIII to XIII show that the condition of nutrition is not an important factor in determining the nerve degeneration and that a reasonable interval (two to forty-eight hours) between death and autopsy does not necessarily mean a sequential myeline sheath change as demonstrated by the Marchi method. (These bodies were kept at a temperature just above freezing.)

The effect of decomposition on nerves was studied by the application of the usual technic to pieces of tissue which have been kept wrapped in muscle at room temperature and fixed at varying intervals. Table XIV shows that degeneration either persists or disappears as decomposition advances.

TABLE XIV.—*Showing the effect of decomposition.*

Autopsy No.	Hours after death.	Degener-ation.	Sheaths.						
5108	8	+	22	-	88	+	-	-	Stained dark.
5118	15	+	84	+	39	-	-	-	Dark and granular.
5120	5	+	9	+	29	-	84	-*	Beaded and frag-mented.
5402	16	+	40	--*	-	-	-	-	Beaded and frag-mented.

\* This disappearance is due to a rapid solution of the reduced osmic acid in the clearing oil.

TABLE XV.—*Degeneration in six decomposed cases studied.*

Autopsy No.	Cause of death.	Degener-ation.	Hours after death.
4548	Submersion .....	-	21
4858	Pulmonary tuberculosis.....	-	40
4864	Generalized tuberculous peritonitis.....	-	12 (?)
4881	Enteritis (cholera) .....	-	31
5003	Submersion .....	-	48
5102	Occipitovertebral dislocation.....	-	(?)

Table XV shows the persistence of degeneration in advanced decomposition.

The results of this work show that degeneration of the myeline sheath in the peripheral nerves in morbidities distinctly non-beriberic is not only present but frequent, and such frequency should always be borne in mind during all post-mortem investigations.

The frequency of degeneration in old age associated with generalized arteriosclerosis and chronic interstitial nephritis, in Asiatic cholera, in pulmonary tuberculosis, in conditions with poor nutrition, and even in apparently healthy individuals killed by accidents is evident, although no definite conclusions could be drawn due to a lack in number in each class of cases studied.

The following explanations have been offered by others as etiological factors in the degeneration of the myeline sheath of peripheral nerves:

1. Degeneration of peripheral nerves may occur in any disturbance of metabolism and nutrition as a result of chemical poisoning or parasitic toxins. (1)
2. Degeneration of peripheral nerves results from a deficiency of a substance or substances necessary for a normal metabolism. (2) (8) (4)
3. Degeneration in apparently healthy individuals is probably due to a one-sided diet (white rice) of the lower class of people to which the

cases studied belong. This explanation is sustained by the experiments in fowl by Vedder and Clark, from which they drew the following conclusions:

- a. Degeneration is present as early as the seventh day of polished rice feeding.
- b. Degeneration may be present without symptoms of neuritis even after thirty-five days of feeding.
- c. Degeneration occurs before the symptoms.
- d. Advanced degeneration may be present with no symptoms of neuritis.
4. Unbalanced diet may be responsible for degeneration in those who died of accidents or diseases of short duration, the degeneration being independent of and preceding the disease.

Osler(4) gives the following causes under the etiology of multiple neuritis:

(a). The poisons of infectious diseases, as in leprosy, diphtheria, typhoid fever, small-pox, scarlet fever, and occasionally in other forms; (b) the organic poisons, comprising the diffusible stimulants, such as alcohol and ether, bisulphide of carbon and naphtha, and the metallic bodies, such as lead, arsenic, and mercury; (c) cachectic conditions, such as occur in anaemia, cancer, tuberculosis, or marasmus from any cause; (d) the endemic neuritis of beri-beri; and (e) lastly, there are cases in which none of these factors prevail, but the disease sets in suddenly after overexertion or exposure to cold.

According to this author neuritis in tuberculosis is not common, while in typhoid fever parenchymatous changes have been met with in the peripheral nerves and appear to be not very uncommon even when there have been no symptoms of neuritis.

In bacillary dysentery peripheral neuritis, though often confined to one nerve, is not uncommon in the mild forms of the disease.(6)

#### SUMMARY AND CONCLUSIONS

1. In a mixed autopsy service in Manila 88 out of 104 cases showed microscopically degeneration of the peripheral nerves by the Marchi method. Of these 88 cases the degeneration was slight in 55, moderate in 29, and marked in 4.

2. Of the 88 cases of nerve degeneration more than half (49) occurred between the ages of 20 and 50 years, but no age was exempt.

3. Of the 88 cases of nerve degeneration 69 had nephritis of some form.

4. The condition of nutrition is not an important factor in determining the nerve degeneration, and a reasonable interval (two to forty-eight hours) between death and autopsy does not necessarily mean a sequential myeline sheath change, as demonstrated by the Marchi method. (These bodies were kept at a temperature just above freezing.)

With the knowledge that this study was made from a routine autopsy service in Manila and that the subjects were all Filipinos, the following factors must be taken into consideration in attempting to explain the occurrence of degeneration in 88 out of 104 cases studied.

1. In Manila beriberi is endemic, and therefore there is the possibility of many unrecognized cases of mild beriberi dying of other diseases.

2. There may be many cases who recovered from beriberi and died of other diseases.

3. The nutrition of the working class of Filipinos in general is below par, due to insufficient food, excessive nonnutritious food, or a one-sided diet.

It is necessary that the clinical history must aid the morbid anatomist in the diagnosis of beriberi. The morbid anatomy of this disease consists of subcutaneous oedema, moistness, congestion, and petechiae of the serous surfaces, marked dilation of the right ventricle with or without hypertrophy, congestion and oedema of the lungs, congestion of the viscera, acute duodenitis, and degeneration of the myeline sheath of the peripheral nerves.

#### REFERENCES

- (1) ANDREWS. *Phil. Journ. Sci., Sec. B* (1912), 7, 67.
- (2) ASCHOFF. *Pathologische Anatomie*. Gustav Fischer, Jena. 3d ed. (1911), 383.
- (3) CASTELLANI and CHALMERS. *Manual of Tropical Medicine*. Ballière, Tindall and Cox, London. 1st ed. (1910), 998.
- (4) OSLER. *The Principles and Practice of Modern Medicine*. D. Appleton & Company. New York and London. 8th ed. (1912), 1021.
- (5) STRONG and CROWELL. *Phil. Journ. Sci., Sec. B* (1912), 7, 271.
- (6) VEDDER and CLARK. *Ibid.* (1912), 7, 423.

## ILLUSTRATIONS

### PLATE I

- Fig. 1. Normal nerve.  
2. Slight degeneration (+) in a case of ulcerative colitis (amœbic).  
3. Moderate degeneration (++) in a case of Asiatic cholera.

### PLATE II

- Fig. 1. Marked degeneration (+++) in a case of acute malaria.  
2. Marked degeneration (+++) in a case of ulcerative endocarditis  
with generalized arteriosclerosis and jaundice.  
3. Moderate degeneration (++) in a case of infantile beriberi.





Fig. 1. Normal nerve.

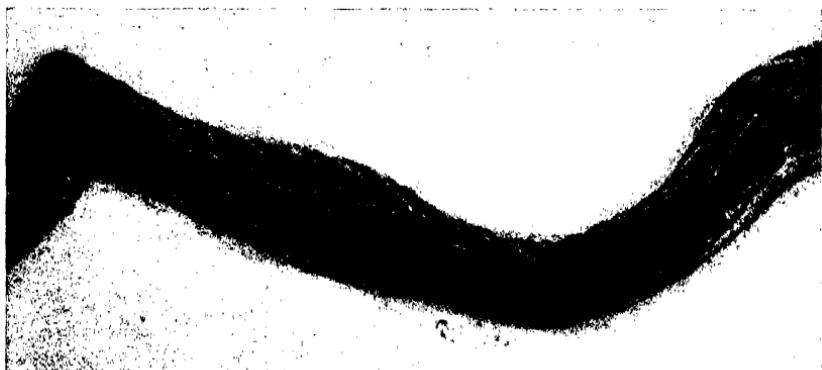


Fig. 2. Slight degeneration (++) in a case of ulcerative colitis (amebic).



Fig. 3. Moderate degeneration (++) in a case of Asiatic cholera.





Fig. 1. Marked degeneration (++) in a case of acute malaria.



Fig. 2. Marked degeneration (++) in a case of ulcerative endocarditis with generalized arteriosclerosis and jaundice.

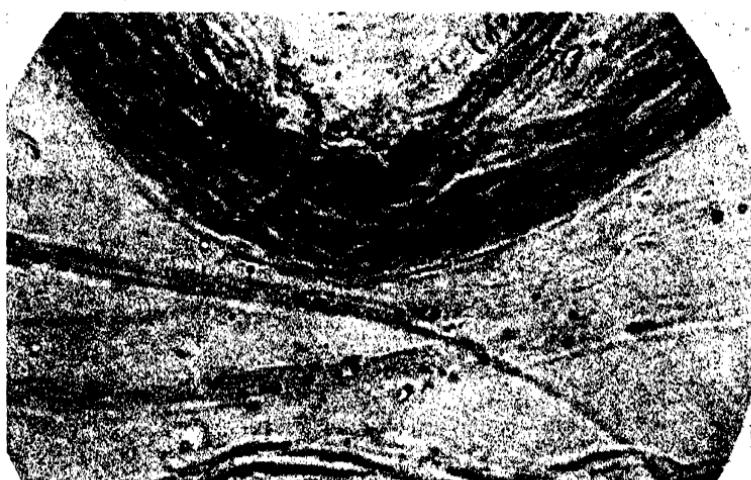


Fig. 3. Moderate degeneration (++) in a case of Infantile beriberi.



## DISAPPEARANCE OF THE PIGMENT IN THE MELANOPHORE OF PHILIPPINE HOUSE LIZARDS<sup>1</sup>

By EDWARD S. RUTH and ROBERT B. GIBSON

(From the Departments of Anatomy and of Physiology, College of Medicine and Surgery, University of the Philippines)

### TWO COLORED PLATES

The literature that has accumulated on the subject of melanophores and chromatophores or pigment-carrying cells is abundant and is chiefly concerned with a discussion of their origin, morphology, and movements (Eycleshymer,(2) Laurens,(6) Spaeth,(10) Lieben,(7) Ballowitz,(1) Hooker,(8) and others). However, the study of the pigment granule, its elaboration, migration, and destruction, has received but comparatively little attention (Von Szily,(11) Redfield,(8) Hooker,(4) and others).

An analysis of the literature indicates that there are at least three different morphological types of melanophores, which Laurens(5) reviews at some length.

Ballowitz \* \* \* reiterates his many times expressed opinion that the movements of the pigment in the pigment cells are due to intracellular streaming in the chromatophores which have unchangeable cell forms. The protoplasm of the chromatophores is filled with numerous extremely fine, radially arranged, anastomosing canals in which the pigment is contained, and which are closed on the outside. No membrane can be demonstrated, but the walls of the canals are extremely thin and are formed by the protoplasm of the chromatophore. The contraction of the protoplasmic walls of the canals, alternating with its relaxation moves and drives forward the pigment granules. If the protoplasmic wall in the processes of the cells contracts in transverse waves from the periphery toward the center, then the pigment streams toward the center of the cell, and the canal protoplasm of the center of the cell disk at the same time relaxing, the pigment streams into it and rounds it off. On the other hand, if the central protoplasm contracts, and the protoplasm of the process relaxes then the melanin granules stream out into the processes.

Spaeth holds to the theory, which is perhaps the most popular, that the chromatophores of fishes are fixed stellate cells within which the pigment is carried in a rather fluid cytoplasm, streams into and out of the processes during expansion and contraction.

Hooker<sup>2</sup> upholds another and third view, that the melanophores of Amphibia \* \* \* lie in preformed spaces and that they expand and contract within the spaces which enclose them. The acts of expansion and

<sup>1</sup> Received for publication January, 15th 1917.

<sup>2</sup> See Hooker, reference No. 3.

contraction, according to this theory, are brought about by pseudopodia, the pigment granules being carried in the cell cytoplasm and the pigment cells are therefore to be considered as amœboid.

In a more recent paper Spaeth<sup>(9)</sup> describes the melanophore as a type of smooth muscle cell and in part concludes—

That in the case of the melanophore there is no direct evidence at hand for a loss or exchange of fluid during contraction. There is, however, a visible and reversible colloidal aggregation of melanin granules following a variety of physiological stimuli all of which elicit contractions in smooth muscle. Similarly a number of physiological stimuli that produce a relaxation in smooth muscle brings about a dispersion of the invisible colloidal particles. The aggregation of melanin granules within the melanophore must therefore be considered a visible expression of the colloidal phenomenon that occurs upon stimulation in the micro-homogeneous colloidal content of smooth muscle cell.

From the above theories and statements it is evident that there is still considerable doubt as to the finer mechanism and nature of the "contraction" and "expansion" of the melanophore, or the aggregation and dispersion of the melanin granules within the cell. Do we after all have more than one morphological type of melanophore, or does some chemical reaction take place in the cell with a subsequent disappearance or reappearance of the pigment granules that may be interpreted as an apparent contraction or expansion of the cell? In a series of experiments we have had occasion to study the pigment cells of Philippine house lizards (*Cosmybotus platurus*, *Peropus mutilatus*, *Hemidactylus frenatus*, and *Hemidactylus luzonensis*—the last very rare), and we have observed that the melanophoric changes in these animals are of a type that does not accord with the descriptions given by investigators who have worked with the other types of melanophores previously mentioned.

Our experiments have been made both upon the living lizard and on isolated pieces of skin that could be studied under the microscope. Some of our observations, along the lines recorded by other investigators, include the results of enucleation of the eyes, decerebration, severing the spinal cord, various kinds of stimulation, and the effects of physiologically active substances such as adrenalin chloride, chloretone, curare, atropine, potassium cyanide, ether, chloroform, carbon monoxide, and isotonic salt solutions.

The change of color in Philippine house lizards is effected fairly rapidly, both from a light to a dark color and vice versa, and the period of time for each change is approximately the same under normal conditions. The variation in color range is merely one of light and dark intensity and includes all the

shades between the two extremes of a creamy white to a taupe (the darkest gray) with a slight brownish tinge. Under normal conditions this lizard changes its color from one extreme to another in about thirty minutes. Upon irritation by shaking in a Petri dish, the time for changing from a dark to a light color can be greatly lessened, approximately fifteen minutes being necessary for the "contraction" of the melanophore. Redfield has observed similar results in the horned toad during states of nervous excitement and believes that this coördination of the contracting melanophore must be due to a hormone, which is probably "adrenin."

A number of experiments were performed to determine, if possible, the normal condition of the melanophore when at rest, whether it was then expanded or contracted. In one series of lizards the eyes were removed under ether anesthesia, while in others the cerebrum was removed, and in still others the spinal cord was severed. The eyeless lizards assumed a dark color irrespective of the color of the background and surroundings.

In the decerebrated lizards similar results were observed both as to their indifference to react to background stimulation, darkness, and light. However, the latter, if mechanically irritated, would always turn a light color, and the melanophores would become "contracted." Laurens says that the eyeless *Amblystoma* larvæ do not respond to difference in background, though they do respond to light stimulation; this is quite the reverse from what is found in lizards. The melanophores of the eyeless *Amblystoma* larvæ, when kept in light, are fully expanded, and when kept in the dark, the subepidermal melanophores are maximally contracted.

If it be true that there is an actual "contraction" and "expansion" of the melanophore, then the aggregated central mass of pigment granules should have greater dimensions in the "contracted" than in the "expanded" cell. In the bleached lizards, many melanophores were seen as minute pigmented points only. Other cells persist, apparently of the normal expanded type, evidently unaffected or only slightly affected in the normal bleaching reflex. However, we have also made measurements of the central masses in such persisting cells in cleared sections of skin; when compared with similar measurements of the central masses of the melanophores of the normally dark lizard, the former were usually less and never greater than the latter.

When cleared sections of dark, light, and the intermediate shades of lizard skin were examined under the oil immersion, the details of the melanophore could be easily seen. The center

of the cell was composed of a mass of pigmented granules; radiating pseudopods filled with granules extended in all directions. In the skin sections taken from lizards in which the melanophores were "contracted," it was observed that the peripheral portion of the pseudopod was composed of *farblose* granules. The melanophore of the lizard is, then, a definite fixed stellate cell composed of granules which may be either pigmented or colorless. "Farblose" and "colorless" are not used in their literal meanings; we use them as terms indicating the appearance of granules that have been depleted of their dark pigment. These bleached granules have a slight yellowish tinge.

Hooker further states,

It may safely be concluded that, in the normal ontogenetic origin of melanin in the frog the chromatin plays no direct role. On the contrary, all the evidence obtained goes to demonstrate that melanin granules are formed in the cytoplasm from elements already present in solution in it, through some action of the nucleus.

To arrive at some definite conclusions regarding these pigmented and farblose granules, a series of experiments was carried out. It was believed that if a means could be found to destroy the pigment, an actual observation could be made under the microscopic. For these experiments small fragments of skin, 4 millimeters square, were removed from the back of a lizard; the pieces of skin were then spread and floated on the surface of an adrenalin solution. The strength of the solution used was 1: 10,000 (1 part of adrenalin chloride to 10,000 parts of Ringer's solution). As soon as the specimen was prepared, it was placed under the microscope and it was observed that the granules in the periphery of the pseudopod gradually began to fade. This fading process progressed rapidly toward the center of the cell. Some melanophores were completely depleted of their pigment, others showed the central pigmented mass remaining, and still others had scattered fragments or groups of pigmented granules separated entirely from the center. The stroma of the pigmented cell remained *in situ*, clearly visible, and of a pale yellow color. These are also shown in the section of cleared skin from the lizard bleached normally within white surroundings (Plate I).

In the above experiments, the skin was floated on the surface of the solution. This was found necessary, since the results were not as constant when fragments of skin were submerged. Local application of adrenalin to the skin of a dark lizard in dark surroundings results in the prompt fading of the area that is moistened by the solution (Plate II, fig. 1).

Lieben was perhaps the first investigator to record the action of adrenalin on the melanophore and states:

Gelegentlich einer Adrenalininjektion bei einem Frosche zum Zwecke der Studiums ihrer Wirkung auf die Gefäße fiel mir auf dass sich die Pigmentzellen sehr bald nach Beginn des Versuches ballten und der ganze Frosch hell wurde.

The adrenalin that we used was diluted in Ringer's solution, 1: 10,000, and 0.1 cubic centimeter was injected into the dorsal lymph sac of a normal dark lizard. Two minutes later there was a distinct blanching of the localized area overlying the injected sac, following which there was a gradual systemic fading of the color of the lizard, so that in from ten to fifteen minutes following the injection the entire skin was a creamy white (Plate II, fig. 2). Throughout the experiment the lizard was kept in dark surroundings. Control animals injected with Ringer's solution and placed in the same chamber showed only a slight fading of the skin immediately surrounding the point of injection. In numerous similar experiments the lizards always reacted promptly when newly prepared adrenalin solutions were employed.

We have tried in many ways to study other conditions that might effect changes in the melanophore. Many of them have been repetitions of those recorded by other investigators. Experiments with ether and chloroform vapor, *in vivo* and *in vitro*, were not conclusive. Carbon monoxide experiments resulted similarly, though dark lizards placed in illuminating gas were slightly bleached because of irritation attending efforts to escape. Adrenalin placed on the skin or injected into the lymph sac was still effective in anaesthetized and carbon monoxide lizards. Skin placed in calcium saline or in potassium saline solution did not change. Experiments with curare, atropine, and potassium cyanide were negative. Application of the tetanizing current to isolated pieces of skin was without effect. Exposure of the lizards to temperatures between 0° and 30° C. produced no change. Dark, dorsal skin, ground with sand and strained through cloth, was not affected by adrenalin. Isolated pieces of skin, killed by exposure to chloroform vapor, did not react to adrenalin.

Some interesting observations were obtained by the administration of chloretone. When light-colored lizards in white surroundings were injected in the dorsal lymph sac with 0.1 cubic centimeter of 1 per cent chloretone solution, the skin overlying the injected area soon became more and more pigmented (Plate II, fig. 4). Subsequently the entire lizard gradually became

darker. The process of pigmentation is much slower than the change from dark to light effected by adrenalin.

The area first darkened by the injection remained well defined in several experiments, indicating a direct effect on the melanophore cells, though positive pigmentation of the granules could not be demonstrated when pieces of light-colored skin were floated on chloretone solution under the microscope. Injection of adrenalin or application of adrenalin to the surface of the skin of chloretanized lizards gives the characteristic bleaching.

#### DISCUSSION

Investigators have heretofore described small pigment-carrying granules in chromatophores and melanophores. Von Szily refers to them as *Pigmentträger* and says:

Die Umwandlung der farblosen Pigmentträger im Pigment erfolgt wahrscheinlich unter dem Einfluss von spezifischen Zellfermenten. Die Letzteren können ihre Wirkung auf das Chromatin, die Muttersubstanz des Pigmentes, erst dann ausüben wenn die Kernmembran normalerweise im Verlaufe der Mitose zeitweise verschwindet, oder wenn einzelne Chromatinpartikelchen in der Teilungsruhe unter den eben beschriebenden Umständen aus dem Kern eliminiert werden.

No other workers have referred to the colorless pigment granules, or farblose Pigmentträger. Hooker and Spaeth seem convinced that there exist in the cytoplasm elements that are capable of combining and by some influence of the nucleus are transformed into melanin granules. Hooker concludes that—

In the cells of embryo frogs, melanin is formed from some substance (probably tyrosine or its derivatives) in solution in the cytoplasm when acted upon by the nucleus (perhaps an oxidase reaction).

What rôle is played by the nucleus in the production of the pigment in the granules of the lizard we are at present not prepared to state. However, studies are now being carried on that may throw more light on this subject. If melanin granules become pigmented by means of an oxidase, we can conceive also of the gradual destruction and disappearance of the pigment by chemical action. This process of destruction and production of pigment explains the apparent "contraction" and "expansion" of the melanophore in the lizard.

Our experiments show conclusively that normally the coördinate fading of the melanophore is due to a primary nervous reflex, through stimulation of the retina, with probably a subsequent production and liberation of a hormone, which is carried about by the blood and lymph. What this hormone is we are

unable to say, though everything points toward "adrenin," as Redfield has previously indicated. Adrenalin has a definite action on the pigment of the melanophore in both the *in vitro* and *in vivo* experiments; there results a gradual fading of the pigment from the periphery toward the center of the cells.

#### CONCLUSIONS

1. The melanophore of Philippine house lizards (*Cosmybotus platurus*, *Peropus mutilatus*, *Hemidactylus frenatus*, and *Hemidactylus luzonensis*) is a definitely fixed stellate cell, which neither contracts nor expands; all pseudopods remain *in situ* during the fading and repigmentation processes.

2. No migration of the pigmented or farblose granules was ever observed either from the center toward the periphery of the cell or vice versa.

3. The pigment in the melanophore of the Philippine house lizards is actually dispersed and disappears from the granule on the application of adrenalin both *in vitro* and *in vivo*, leaving a definite farblose granule which can be seen with high magnification. The same farblose granules are also seen in the melanophores of the lizard bleached by white surroundings.

4. It may be assumed that the disappearance of the pigment of the granules is an intracellular chemical change, which seems to occur when the melanophore is stimulated by a hormone (probably adrenin); the pigmented state is the normal condition, the melanophore *in vivo* elaborating the pigment when the reflex secretion of the hormone is discontinued.

#### REFERENCES

- (1) BALLOWITZ, E. Über die Pigmentströmung in die Farbstoffzellen und die Kanälchenstruktur des Chromatophoren-Protoplasmas. *Pflüger's Arch.* (1914), 157, 165-210.
- (2) EYCLESHYMER, A. C. The development of chromatophores in *Necturus*. *Am. Journ. Anat.* (1906), 5, 309-318.
- (3) HOOKER, D. Amœboid movement in the corial melanophores of *Rana*. *Am. Journ. Anat.* (1914), 16, 237-250.
- (4) IDEM. The rôles of nucleus and cytoplasm in melanin elaboration. *Anat. Rec.* (1915), 9, 393.
- (5) LAURENS, H. The reaction of the melanophores of *Ambystoma larvæ*. *Journ. Exp. Zool.* (1915), 18, 577.
- (6) IDEM. The reactions of the melanophores of *Ambystoma larvæ*—The supposed influence of the pineal organ. *Journ. Exp. Zool.* (1916), 20, 237.
- (7) LIEBEN, S. Über die Wirkung von Extrakten chromaffinen Gewebes (adrenalin) auf die Pigmentzellen. *Centralbl. f. Physiol.* (1906), 20, 108.

- (8) REDFIELD, A. C. The coordination of chromatophores by hormones. *Science* (1916), n. s. 42, 580.
- (9) SPAETH, R. A. Evidence proving the melanophore to be a disguised type of smooth muscle cell. *Journ. Exp. Zool.* (1916), 20, 193.
- (10) IDEM. The mechanism of the contraction in the melanophores of fishes. *Anat. Anz.* (1913), 44, 520-524.
- (11) VON SZILY, A. Über die Entstehung des melanotischen Pigments im Auge der Wirbeltierenembryonen und in Choroidealsarkomen. *Arch. f. mik. Anat.* (1911), 77, 1. Abt., 87.

## ILLUSTRATIONS

### PLATE I

[Drawing by Julian Castro.]

A camera lucida drawing of a melanophore of a Philippine house lizard, showing both the pigmented and the colorless granules in the radiating pseudopods. No. 3 ocular,  $\frac{1}{12}$  oil immersion objective, reduced about one third.

### PLATE II

- Fig. 1. A house lizard, showing the bleaching of the skin five minutes after the application of adrenalin.  
2. A house lizard partly bleached by the injection of 0.1 cubic centimeter of adrenalin chloride (1:10,000) into the posterior lymph sac. The lizards shown in figs. 1 and 2 were kept in the same dark cage during the experiment.  
3. A normal dark lizard.  
4. A normal bleached lizard ten minutes after an injection of 0.1 cubic centimeter of 1 per cent chloretoe in the right posterior lymph sac; the darkened area of skin overlies the injected lymph sac.  
5. A normal lizard partly bleached by being kept in white surroundings.



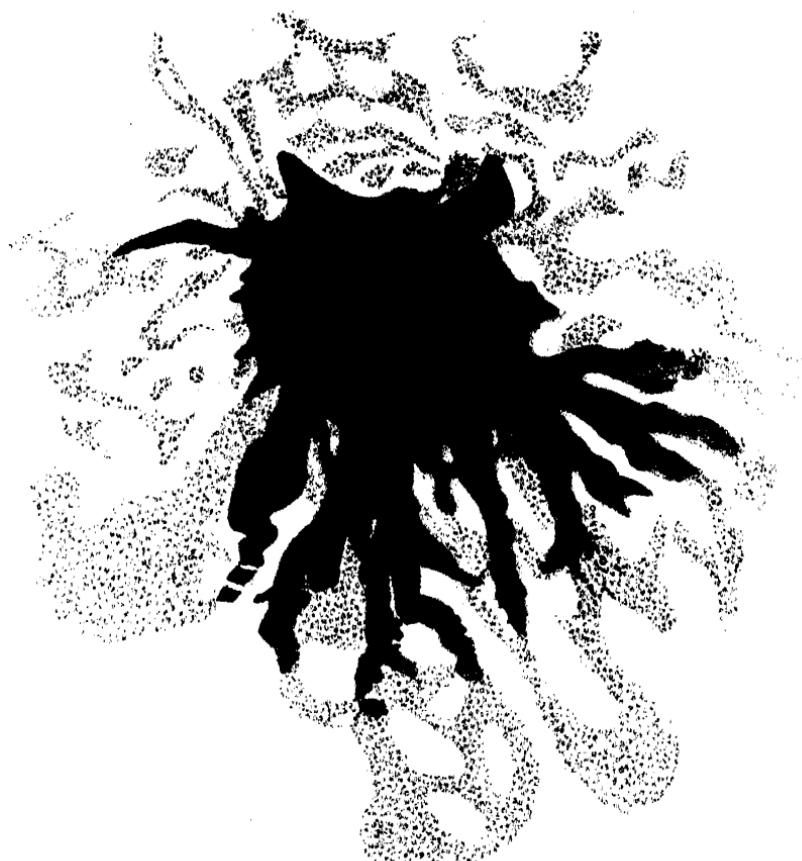


PLATE I. A MELANOPHORE OF A HOUSE LIZARD.



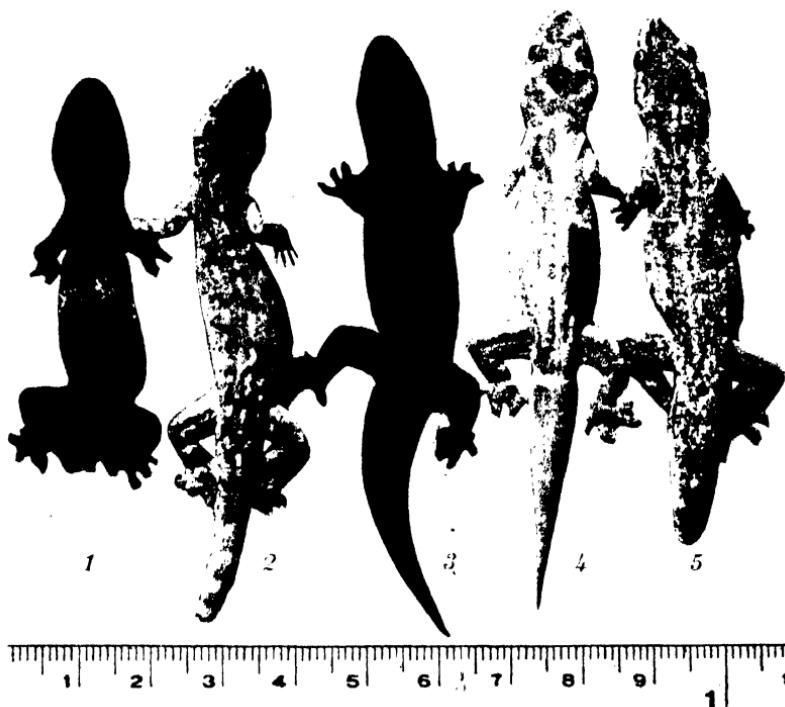


PLATE II. PHILIPPINE HOUSE LIZARDS.



## ESSENTIAL FACTOR IN THE TREATMENT OF PREGNANT CHOLERA PATIENTS<sup>1</sup>

BY PAUL MCC. LOWELL  
*(Philippine Health Service, Manila)*

Among the many incidents that a physician treating cholera has to contend with none, perhaps, will cause him more anxiety than the handling of the pregnant woman. The almost hopeless condition of coma in some and delirium in others, so striking at times, often causes him to give them less attention than they deserve. For over a century men have written about cholera, describing the clinical picture, and have often mentioned the pregnant cases, comparing their chances for recovery with those of the nonpregnant. However, the different workers contended with unlike conditions, and their methods of treatment varied greatly; consequently their results and deductions are so non-uniform that considerable doubt is left in one's mind as to the correct prognosis of these cases. It is evident that in order to obtain satisfactory deductions one must treat a sufficient number of these cases, of varying virulence, extending over a considerable period, and not be misled by the prognosis obtained in small epidemics.

In Manila we have had admissions of cholera to San Lazaro Hospital almost continuously from September, 1913, to February, 1917, of a spasmodic virulence varying at times from a very severe typical type to a more or less mild atypical one. The cholera here is thought by some to be endemic, and the admissions during this period numbered 1,588, all of which were Filipinos residing in Manila or its near vicinity. Of these, 379 were females between the ages of 15 and 40, and 77 of this number were pregnant, which were distributed as follows: 4 cases were pregnant for two months; 13 for three months; 4 for four months; 13 for five months; 9 for six months; 14 for seven months; 11 for eight months; and 9 for nine months.

Sixty-six of these cases received the ordinary treatment of (1) intravenous injections of a hypertonic salt solution containing soda bicarbonate and (2) the usual symptomatic treatment when

<sup>1</sup> Submitted as a thesis for the degree of Doctor of Public Health. Received for publication April, 1917.

indicated, resulting in 36 recoveries and 30 deaths, which gave a mortality of 45 per cent. This mortality is indeed high when compared with the 19 per cent obtained from the identical treatment in the 302 nonpregnant cases, that is, 245 recoveries and 57 deaths as tabulated in Table I.

TABLE I.—*Showing the admissions, recoveries, deaths, and mortality of the pregnant and the nonpregnant cases under discussion.*

	Admis- sions.	Recov- eries.	Deaths.	Mortal- ity.
				Per cent.
Nonpregnant.....	802	245	57	19
Pregnant.....	•66	36	30	45
Total.....	868	281	87	23

\* Eleven cases are excluded for later consideration.

These results compel me to disagree with Kovalsky,(10) who states that the mortality in the pregnant cases is not much higher than in the nonpregnant ones. Davis(3) is of the same opinion, in that cholera does not materially increase the mortality, whereas Basil(1) states that when the pregnancy is far advanced in a cholera case it adds much to the gravity of the condition. Hirsch(8) obtained a mortality of 54 per cent; Bouchut,(2) 56 per cent; Härtén,(7) in Utrecht, 58 per cent; and Freschi,(5) in Genoa, saw nearly all the pregnant cases die. Nichols and Andrews,(12) from their experiences in San Lazaro Hospital, Manila, in 1908, think that as much as pregnancy lessens the chances of the patient's recovery such cases do not necessarily prove fatal. Schütz's(16) results show a mortality of 57 per cent for the pregnant cholera patients, and he thinks that this mortality is in direct proportion to the lateness of the pregnancy. It is evident, as shown in Table I, that the chances for recovery of the pregnant cholera patient are decreased by more than twofold. These results agree with those of Liebermeister,(11) who states that pregnancy greatly increases the danger to the life of the mother.

Some authorities call attention to the fact that in cholera, in general, the mortality depends upon the interval between the attack and the time of receiving treatment. For the present 66 cases, the average interval for those who died was twenty-five hours, and for those who recovered it was fourteen hours. Most of the patients were admitted in the stage of evacuation, that is, the first stage of the disease, and the low mortality of only

17 per cent obtained for this period can be explained by the fact that the treatment administered to the cases in this period carried many over it that would have otherwise died in it. The mortality for the algid stage was 65 per cent, an important fact, which will be referred to later on, and for the third period, or the stage of reaction, it was 18 per cent.

When one considers that the system is greatly taxed during cholera and that the continuation of the pregnancy is in danger, as is found in the other acute infections, one must naturally expect abortions to occur. This was true in the present series of 66 cases, which gave a total of 37 abortions (56 per cent), which can be favorably compared with the 50 per cent reported by Bouchut.(2) For the sake of clearness the term "abortion" is used to denote any kind of delivery at any month. Liebermeister<sup>(11)</sup> and Nichols and Andrews<sup>(12)</sup> agree that the pregnant cholera patients usually abort. Hirsch,<sup>(8)</sup> in his summary of cases in 1854, gives a high percentage (78 per cent); 17 of his 25 cases aborted. Schütz<sup>(16)</sup> reports 52 abortions in 115 cases (45 per cent), calling attention to the tendency to abort more frequently as the pregnancy is advanced, which condition was present in this series, as is illustrated in Table II, but not in the arithmetical progression as stated by Schütz.

As to the stages of the disease when abortion most frequently occurs, Liebermeister<sup>(11)</sup> states that if the mother does not succumb she usually aborts during the period of reaction. The present series of cases does not support this statement, as 5 per cent of the foetuses were delivered in the first stage of the disease, 75 per cent in the second, and 20 per cent in the third. In 1892 Klautsch<sup>(9)</sup> saw in Hamburg 10 pregnant cholera cases abort in the second stage of the disease. These results are further supported by Davis,<sup>(3)</sup> who claims that the foetuses usually die in the second stage, the abortions setting in during the same period.

Of the 66 cases of pregnancy in the present series, 37 aborted, of which only 2 foetuses were born alive, one of which died within a few hours after delivery, and the other was discharged from the hospital alive with the mother. All other cases were either born dead or before the age of viability; adding to this number those that died with the mother, we obtain a total of 49 foetal deaths in 66 pregnancies (71 per cent). Kovalsky<sup>(10)</sup> states that over 80 per cent of the pregnancies in his cases came to an untimely end, and Bouchut<sup>(2)</sup> and Hirsch<sup>(8)</sup> saw equal fatal results (80 per cent) in their respective experiences.

Klautsch(9) saw 10 pregnant cases admitted to the hospital and all the foetuses were born dead, while Schütz(16) reports that most (75 per cent) of his birth cases were stillborn. All these different observers agree that abortions are very frequent in cholera and that the foetuses are rarely born alive. The fact that pregnant women who survive an attack of cholera later on abort, or that the children when born show any effect of the cholera with which the mother was attacked when pregnant, is contrary to the opinions of Davis(3) and Basil.(1) However, no extensive observations have been made in the present series touching on this point.

TABLE II.—*Showing foetal and maternal mortality in pregnant cholera patients.*

	Months of pregnancy.								Total.
	2d.	3d.	4th.	5th.	6th.	7th.	8th.	9th.	
<b>Patients who aborted:</b>									
Deaths .....	2	1	1	3	2	2	5	2	18
Recoveries .....	0	4	1	4	3	1	0	6	19
Mortality for the mother ..... per cent..	100	20	50	48	40	66	100	25	49
Average percentage for the first four months, the second four months, and the ninth month			44				60	25	49
<b>Patients who did not abort:</b>									
Deaths .....	0	3	0	1	2	3	2	1	12
Recoveries .....	2	4	1	2	2	4	2	0	17
Mortality for the mother ..... per cent..	0	48	0	38	50	48	50	100	42
Average percentage for the first four months, the second four months, and the ninth month			30				40	100	42
<b>Sum total for both:</b>									
Total mortality for the mothers ..... per cent..	50	33	33	40	44	50	77	33	45
Total mortality for foetus- es ..... per cent..	50	66	66	80	78	60	77	88	71
Tendency to abort. percent	50	42	38	70	56	30	55	90	56
Average percentage of abortions for the first and second periods of the pregnancies .....			47					60	

All observers seem to agree that the weakness and the toxic condition of the mother causes a protracted and irregular delivery, which is more pronounced the longer the period of pregnancy

and the greater the severity of the case. The foetuses are usually cyanotic and often show various degrees of maceration, thus indicating that death had taken place a considerable time previous to the delivery. As a rule, the foetus, membranes, and placenta were delivered intact in direct proportion to the severity of the patient's condition and inversely to the period of gestation.

Therefore, if abortions occur in the majority of the cases of cholera and the foetuses are stillborn, what effect do they have on the mortality of the mother? Galliard and Schütz(6) saw the majority of pregnant cholera cases die after abortion had taken place. Rumpf(14) entertains a similar opinion to Bouchut,(2) who states that abortion offers an unfavorable prognosis for the mother. Table II shows the aborting cases in the present series, which resulted in a mortality of 49 per cent for the mother, and in those cases in which abortion did not occur, 42 per cent of the mothers died. Hirsch's(8) results are almost equal for those who did not abort (63 per cent) and for those who did abort (65 per cent), but Schütz(16) obtained a much greater mortality for those who did abort, that is, 62 per cent in comparison with the 44 per cent mortality for those who did not abort.

From these percentages it seems that the patients who aborted thereby decreased their chances for recovery, whereas those who did not abort had a better prognosis and kept their foetuses intact. But my clinical observations have inclined me to believe otherwise, and this belief is strengthened by a study of the figures of Bouchut,(2) who states that of his 18 cases which aborted only 9 died, while 19 of the 25 which did not abort died. I am convinced that the abortion is a life-saving measure for the mother when it occurs in time, although the high percentage of mortality as given by others seems to indicate the contrary. This act of abortion is a possible factor for recovery in the severe form of the disease and unnecessary in the mild form. Can we conclude that such cases would not have terminated fatally if they had not aborted? The fact that it required an average period of 9.6 days in order to recover in those cases that did abort in comparison with the average of 7.3 days required for recovery in the cases that did not abort does not signify that the abortion retarded the recovery, but indicates that this class of patients was of a more serious type. Although many died after abortion, it does not necessarily mean that the abortion was a cause of it but an effect of the disease and a necessary requirement for recovery and that the abortion

occurred too late to be of any avail, as the period between the admission to the hospital and the time of the abortion was an average of thirty-one hours for the fatal cases and twenty-two hours for those who recovered. The retardation of the abortion in the fatal cases naturally caused the delivery to take place at a time when the patient's condition was at the weakest, when more toxins had been absorbed from the dead foetus, and when the energy expended in the process was sufficient completely to exhaust the mother. This was strikingly illustrated in a number of cases in which the last effort, voluntary and involuntary, made by the patient in this world was to rid herself of her dead foetus. Further the percentage of mortality for the mother observed in favor of the cases that did not abort is in itself a proof that this class of cases was of a milder form, that the mother was not absorbing any toxins from a dead foetus to aggravate her already serious condition, and that the energy not expended in delivering a foetus was reserved for the recovery of herself.

The fact that the mortality for the mother is increased proportionately to the term of the pregnancy, as seen in Table II, agrees with a similar statement made by Schütz.(16) The mortality of the mothers (60 per cent) aborting foetuses ranging from the fourth to the ninth month is greater than for the period before the fourth month (44 per cent). The larger the foetus, the greater the tax required by the mother in its expulsion, thus lengthening the process of the delivery. The more fully developed placental circulation and the firmer attachment of the placenta during the latter months of pregnancy facilitate the absorption of toxin originating in the dead foetus before its separation occurs, thus rendering more unfavorable the mother's prognosis.

The mortality of 50 per cent for the mother for the total of the second month of pregnancy (Table II) brings to one's mind the idea of toxæmia of pregnancy so frequently seen in early pregnancies in general, causing the cholera patient a graver prognosis, while those of the ninth month, being so near term, cause no additional strain on the mother, as convincingly seen in the resulting mortality of only 33 per cent in 10 cases. It was in this group of cases that a child was born alive to be discharged from the hospital with its mother.

From the foregoing it is evident that abortions are very frequent in cholera patients, that the mortality is very much higher in the pregnant cases, and also that the foetuses are nearly all stillborn. The question arises, What kills the foetus?

TABLE III.—Showing 66 cases divided into 6 groups, based upon the presence or absence of the radial pulse on admission and the interval between the admission and the appearance of urine.

	Radial pulse present on admission.	Radial pulse not present on admission.
Urination on admission.	(Group No. I): 23 cases; 11 abortions (48 per cent); mortality of cases, 17 per cent.	(Group No. VI): No cases in this group.
Urination was present within 24 hours after admission.	(Group No. II): 8 cases; 5 abortions (62 per cent); mortality of cases, 18 per cent.	(Group No. V): 4 cases; 3 abortions (75 per cent); mortality of cases, 50 per cent.
Urination was not present within 24 hours after admission.	(Group No. III): 21 cases; 11 abortions (52 per cent); mortality of cases, 66 per cent.	(Group No. IV): 10 cases; 7 abortions (70 per cent); mortality of cases, 80 per cent.

Group I comprised 23 cases, which had a radial pulse and urinated on admission. Of this class 17 per cent died and 48 per cent aborted.

Group II comprised 8 cases, which had a radial pulse and did not urinate on admission, but did urinate within twenty-four hours. This group showed a mortality of 18 per cent; 62 per cent aborted.

Group III comprised 21 cases, which had a radial pulse on admission, but did not urinate within twenty-four hours. The mortality for the mother was 66 per cent; 52 per cent aborted.

Group IV comprised 10 cases, which did not have a radial pulse on admission and did not urinate within twenty-four hours. The total mortality of this group was 80 per cent. Seven of the 10 cases aborted (70 per cent), and three cases did not. This group is interesting, because it portrays the worst prognosis and because the three cases that did not abort died. The two cases that aborted and recovered were pregnant for less than four months.

Group V comprised 4 cases, which had no radial pulse on admission, but urinated within twenty-four hours. The mortality for the mothers was 50 per cent, and 75 per cent aborted.

For completeness group VI was made to show the outcome of the cases which had no radial pulse but urinated on admission. As no such condition can reasonably exist, no cases were found to represent this group.

Rogers(13) has proved that by lowering the specific gravity of the blood to normal by the addition of a solution which thereby restores the blood to its normal volume and so increases the arterial pressure many patients who upon admission are pulse-

less and fail to urinate can be made to do so in a short time. Therefore the absence of urine in the early stage of cholera must be a mechanical process resulting from the fluid portion of the blood becoming decreased, and hence the remaining blood, of higher specific gravity and decreased volume, is unable to circulate through the secreting tubules of the kidneys, resulting in the cessation of urinary secretion. Then the same principle must apply to the arterial system of the uterus. If this failure of the circulation lasts sufficiently long, the foetus must surely die, because the mother's blood fails to nourish it and to carry off the waste products, thus allowing the toxins to accumulate in it. Also the failure of the mother to eliminate properly results in the damming up of her own toxins to the detriment of the foetus.

These factors alone are sufficient reasons for the subsequent death of the foetus and for the high percentage of abortions as seen in group III. But then, what justifiable reasons can be given for the cases comprising group I, which cases never became pulseless and did urinate on admission, showing 48 per cent abortions in contrast with group III, which cases did not urinate on admission and gave 52 per cent abortions, a difference of only 4 per cent. Then if the cessation of urination in the early stage does not cause abortion, and as the period of the fever before abortion occurs is so short, it does not seem possible for the same factor which causes the abortions in the other fevers to be responsible. Sellards<sup>(17)</sup> has proved the presence of an acidosis in cholera, and Rogers<sup>(18)</sup> states that this acidosis is an important factor in causing postcholeraic uræmia. Davis<sup>(3)</sup> says that the placenta is affected and that the foetal movements are unusually violent during the first stage, and my own observations agree with this statement. Schütz<sup>(16)</sup> found that cholera shows a marked tendency to affect the nonpregnant uterus, particularly in the first stage, producing a metrorrhagia in one third of the cases, but that the Graafian follicles show no signs of a hemorrhagic condition, thus dispelling the idea that this metrorrhagia may be a menstruation. This condition was not often noticed in the present series of cases, but the necropsy reports of the nonpregnant cases, many of which were not admitted to the hospital and were untreated by intravenous injections, showed that hemorrhage in the uterine cavity, hemorrhagic endometritis, and congestion of the serosa of the uterus, ovaries, and fallopian tubes were not uncommon. Slavjansky<sup>(15)</sup> has described a hemorrhagic endometritis in one third of his nonpregnant cases.

Williams(19) states that in nearly every instance the disease causes uterine contractions, resulting from the toxins in the blood. Expecting then a similar change in the pregnant uterus, a high percentage of abortions is sure to occur, and as it has been shown that they occur mostly in the second stage of the disease, the foetus-killing factor must necessarily act very early in the first stage before the patient becomes pulseless, and so if, on admission, the foetus is dead and any assistance is to be rendered to the mother, it must be given as early as possible, in order to cause the absorption of a minimum amount of foetal toxins and also to cause the exhaustion of the smallest possible amount of energy in the delivery of the foetus.

In the latter part of 1916 the cholera admissions increased, and the pregnant cases were frequently examined to ascertain if the foetus was dead or if abortion was in progress. If either of these two conditions was present, then such assistance was given as indicated by the severity of the cases (Table IV).

TABLE IV.—*Eleven cases in which dilatation of the cervix uteri or dilatation and extraction were performed.*

Cholera case No.	Age.	Interval between attack and admission. <i>Hours.</i>	Pulse on admission.	Urination on admission.	Manner of treatment.	Month of pregnancy.	Recovered in-- <i>Days.</i>	Died of
6159	21	4	Present	Absent	Dilatation and extraction.	7	7	
6170	23	7	do	do	do	5	7	
6189	30	36	do	do	do	7	10	
6197	26	8	Absent	do	Dilatation	4	6	
6382	30	8	Present	do	do	5	9	
6346	30	12	Absent	do	Dilatation and extraction.	7		Pneumonia 29 days after.
6381	18	18	Present	Present	do	8	6	
6395	20	4	Absent	Absent	do	7		Uraemia 12 days later.
6439	24	?	Present	do	Dilatation	8	10	
6418	21	5	Absent	do	Dilatation and extraction.	8	9	
6443	25	12	Present	do	Dilatation	5	12	

\* Foetus was alive when born.

The above 11 cases of pregnant cholera women, in which ten of the foetuses were dead, were aided either by dilatation of the cervix uteri alone or by dilatation and extraction of the foetus. All were in a very serious condition. In 7 of these, dilatation and extraction were performed. The average age was 24 years;

the average period of pregnancy was 5.7 months; the average interval from the beginning of the attack until admission to the hospital was only 10.5 hours, a substantiating fact that the foetuses are killed early in the first stage of the disease. Two cases in which dilatation and extraction were performed died, one of pneumonia twenty-seven days later and the other of uræmia nine days later. The latter patient had passed a normal amount of urine for four days and was on full diet for two days, when she developed such a severe case of uræmia that all our efforts failed to save her. All the other cases made uneventful recoveries.

In the cases in which dilatation and extraction were performed, the whole operation did not take more than fifteen minutes for any one case. No anaesthesia was necessary, as the patients were in the partially comatose state seen so frequently in cholera. Also, as the tissues were very lax, the cervix uteri was very easily dilated, and the shock to the mother was practically nil. The foetuses with one exception were dead when removed and showed no signs of maceration. The amniotic fluid was almost normal in amount, and the after-delivery bleeding was always very scant, except in the case of the birth of the live foetus, in which it was slight. The procedure in the last-mentioned case was resorted to because abortion was in progress, and if not speedily terminated, the patient would have died.

The mortality of these 11 cases was 18 per cent, which is about the same obtained in the nonpregnant cases in this hospital (19 per cent), thus giving the pregnant patient the same chance for recovery as the nonpregnant. This procedure prevented the mortality of 45 per cent, which was obtained in the pregnant cases not treated in this manner. The average period of recovery was 8.7 days, which, although not as low as the average 7.3 days that was obtained in those cases that did not abort, is lower than the average in those cases that did abort without this procedure, which was 9.6 days.

Nichols<sup>(12)</sup> prefers not to interfere with the pregnant condition of cholera patients on the grounds that they are not strong enough to withstand the shock. This is very true at times if the interference is not resorted to until the patient is in an extremely serious condition, as I have seen on three occasions. Basil<sup>(1)</sup> states that he cannot follow the advice of some of the continental authorities who advocate emptying the uterus in all cases. This seems to be unwise, as there is a class of patients who will recover without this procedure. During

this same period there were also admitted 6 cases whose condition was such that the pregnancy showed no signs of being interrupted, and they all were discharged with their foetuses intact. French(4) agrees with Basil(1) and states that convalescence is delayed when the pregnancy is interrupted, but in the strict sense of the word none of these cases was interrupted, but the mother was simply helped to remove the dead foetus, which, if she were left alone, would have in all probability taxed her strength to the limit to have delivered it later, and in the meantime she would have absorbed its toxins to her own detriment.

From the facts narrated above, it is evident that the speedy termination of attempted abortion, or the removal of the dead foetus, is not only justified but indicated. Even if the number of cases experimented upon may seem to be small, I think it is sufficiently large when considering the results obtained. The almost immediate urination following and the general change in the condition for the better after the delivery were at times nothing short of marvelous.

This method seems to be original, as I am unable to find any mention of it in the literature available, with the possible exception of Davis,(8) who advocates the speedy termination of the labor if it should start, but says nothing about removing the dead foetus when abortion is not threatened.

#### CONCLUSIONS

1. Pregnant cholera cases have a higher mortality than non-pregnant cases, if left to their own resources.
2. The later the pregnancy the graver is the prognosis for the mother.
3. There is some factor other than mechanical which kills the foetus very early in the disease in the majority of the cases.
4. Abortions occur in most of the cases, and the older the foetus the greater is the tendency to abort.
5. Most of the pregnancies come to a fatal termination.
6. Abortion is nature's therapeutic measure in aiding the mother in her fight for life.
7. The essential factor in the treatment of pregnant cholera cases is to remove the dead foetus as soon as possible and in the manner best suited to the mother's condition, because it shortens the period of convalescence, preserves the strength of the mother, and reduces the mortality to about that of the nonpregnant cases.

**REFERENCES**

- (1) BASIL. *Brit. Med. Journ.* (1910), 2, 840.
- (2) BOUCHUT. See 18.
- (3) DAVIS. Treatise on Obstetrics. Lea Bros. & Co., Philadelphia and New York (1896), 169.
- (4) FRENCH, H. *Lancet* (1908), 1, 1897.
- (5) FRESCHLI. See 18.
- (6) GALLIARD and SCHÜTZ. See 18.
- (7) HÄRTEN. See 18.
- (8) HIESCH. See 18.
- (9) KLAUTSCH. See 18.
- (10) KOVALSKY. See 4.
- (11) LIEBERMEISTER, C. Nothnagel's Encyclopedia of Practical Medicine. Am. ed., W. B. Saunders & Co., Philadelphia and London (1902), 381.
- (12) NICHOLS and ANDREWS. *Phil. Journ. Sci., Sec. B* (1909), 4, 90.
- (13) ROGERS. *Ind. Med. Gaz.* (1916), 7.
- (14) RUMPF. Twentieth Century Practice of Medicine. W. Wood & Co., New York (1901), 14, 374.
- (15) SLAVJANSKY. See 18.
- (16) SCHÜTZ. *Centralbl. f. Gyn.* (1894), 18, 1138.
- (17) SELLARDS. *Am. Journ. Trop. Dis. & Prev. Med.* (1914), 2, 104.
- (18) STICKER, G. Abhandlungen aus der Seuchengeschichte und Seuchenlehre. Verlag von A. Töpelmann, Giessen (1912), 428.
- (19) WILLIAMS. Obstetrics. D. Appleton & Co., New York and London (1910), 482.

# ECHINOSTOMA ILOCANUM (GARRISON): A REPORT OF FIVE CASES AND A CONTRIBUTION TO THE ANATOMY OF THE FLUKE<sup>1</sup>

By J. S. HILARIO<sup>2</sup> and L. D. WHARTON<sup>3</sup>

(From the Departments of Pathology and Medical Zoölogy, University of the Philippines)

ONE PLATE AND ONE TEXT FIGURE

In October, 1916, an ovum was found in the clinical laboratory of the Philippine General Hospital, Manila, measuring 90 microns in length and 50 microns in width and bearing the same morphological characteristics as described by Garrison in 1907.

It is oval in shape with one end more sharply rounded; the shell is light brown in color, smooth and rather delicate, with an operculum at the sharper end; the contents are rather refractile, colorless, and composed of a mass of yolk-cells, among which the germ cell could in some cases be recognized.

Large numbers of ova of this description were collected from the first two cases, and they were placed in distilled water and in saline solution and were preserved in alcohol after fixation in acetic sublimate.

After a careful study of the material on hand a tentative diagnosis of *Echinostoma ilocanum* was made, which was later confirmed by Professor Crowell and one of us (Wharton) in a fresh specimen.

Through the courtesy of Dr. E. Domingo, from the department of medicine, it was possible for us to secure the worms after a dose of male fern. Eight worms were obtained from the first case, the specimen of stool from the second case failing to show any. The treatment consisted of 24 capsules of oleoresin of male fern given in doses of 4 capsules every ten minutes. During the previous day the patient was kept on liquid diet without milk as a preparatory measure for the next day's treatment.

The detection of the worm in the stool is fraught with no little difficulty on account of its small size, its flat body, and its appearance, which makes it hardly distinguishable from the small parti-

<sup>1</sup> Received for publication April, 1917.

<sup>2</sup> Assistant professor of pathology.

<sup>3</sup> Assistant professor of zoölogy.

cles of faecal matter. This is especially true if the worm is more or less decomposed, when it is rather flabby and pale; it is relatively easily recognizable when fresh or when suspended in formalin solution as passed with the stool. It then shows a grayish color, usually with injected coils along the median line, plainly visible through the cuticle.

To obtain better specimens than the first eight, on which no spines on the cuticle were seen, as described by Odhner, except one, which showed them around the oval sucker, male fern was again given the same two patients from whom we secured the first batch of worms. This time the stools were collected in vessels containing 10 per cent formalin solution, and eight apparently well preserved flukes were recovered from both. They were immediately examined under the microscope; only one showed cuticular spines. In December, 1916, ova of identical description were found again in the course of routine examination of faeces from three charity patients, who were admitted in the free wards for diseases alien to the presence of the worm in the intestines, such as adenocystoma of ovary. Of these only one was treated with male fern, but the specimen was lost, owing to a mistake on the part of the personnel in charge, and further treatment could not be undertaken because of the patient's poor condition.

The symptoms presented by these five cases at the time their stools were examined were anaemia, fairly marked in one of them, with occasional headache and dizziness. The blood picture showed no other changes, outside of a more or less marked decrease of the haemoglobin percentage, moderate diminution in number of red blood corpuscles, and eosinophilia in some cases. In two cases *Ascaris* and *Trichuris* ova were found as well; in one case, *Ascaris*, *Trichuris*, and hookworm, and in two the fluke was present alone. All the cases are natives of Zambales, Luzon, the towns whence they came being San Felipe, San Antonio, San Narciso, and Cabanagan.

No definite pathological changes have been described as yet as being brought about by the invasion of the intestines by this worm. The fact that it apparently thrives on the host's blood, as shown by the constant presence in the hosts of varying degrees of anaemia associated with reflex symptoms and slight variation in the blood picture peculiar to blood-sucking intestinal parasites, and the perfusion of the digestive tract of the fluke, which has been observed on examination of the fresh specimen, are very significant.

That the fluke is a common parasite in the intestines of natives

of Zambales, we believe, is not to be questioned. The fact that all our cases came from that province tempts us to assume that the parasite may be just as prevalent there as in Ilocos Sur, which is the locality established by Garrison on the basis of the fact that all his cases were obtained from there. In this connection further work on geographical distribution of the fluke may show, in the face of the conflicting findings as to locality, wider fields of distribution than is even now suspected.

#### REPORT OF CASES

*Case 1.*—I. F., female, 20 years old, born and living in San Felipe, Zambales, entered the School of Nursing July, 1916. She is moderately well nourished, but very pale. She complains of constipation, headache, and occasional dizziness. Blood examination shows 65 per cent haemoglobin, 4,800,000 erythrocytes, 8,600 leucocytes, 78 polymorphonuclear neutrophiles, 20 lymphocytes, 8 polymorphonuclear eosinophiles, 4 large mononuclears. In October, 1916, in the routine examination of the stool, a moderate number of ova of *Echinostoma ilocanum* was encountered. After giving a dose of oleoresin of male fern, 8 worms were obtained, in apparently poor condition. On January 21, 1917, the treatment was repeated and the stool was collected in a dish containing 10 per cent formalin. Five worms in apparently good condition were passed. Of these only one exhibited cuticular spines. The specimen was fixed in formalin solution.

*Case 2.*—T. M., female, 21 years old, native of, and residing in, San Antonio, Zambales, entered the Philippine General Hospital as a probationary student in the School of Nursing on July, 1916. She is well nourished and well developed, but somewhat pale. She complains of occasional headache, sometimes stomach ache, regularly slight constipation, and irregular menses. Blood examination showed 85 per cent haemoglobin, 5,400,000 red blood cells, 11,600 leucocytes, 78 polymorphonuclear neutrophiles, 15 lymphocytes, 6 large mononuclears, and 1 eosinophile. In November, 1916, the examination of the stool showed rare ova of *Echinostoma*, as also a few eggs of *Ascaris* and *Trichuris*. She was given a treatment of male fern. After a careful examination of the stool no worms were found. On January 21, 1917, another dose of male fern was administered, and the stool was directly received in a solution of formalin. Three worms were recovered.

*Case 3.*—(Case 47963) P. C., 38 years old, female, married, born and living in Cabangan, Zambales, admitted to the Philippine General Hospital for enlarged abdomen. She is fairly well

developed, but much emaciated, with oedema of the limbs. Laparotomy showed a large tumor in the region of the ovary. On January 18 the stool was sent in for routine examination. A few ova of *Echinostoma ilocanum* were found. Male fern treatment was given, but for reasons already set forth, the specimen of stool collected was not examined for the worm.

*Case 4.*—(Case 6920) C. V., male, 10 years old, born and residing in San Narciso, Zambales, admitted to the Philippine General Hospital complaining of yaws. He is fairly well developed and well nourished, but somewhat pale. Blood picture shows 75 per cent haemoglobin; otherwise it is normal. On December 7 examination of the stool showed a few eggs of *Echinostoma ilocanum*. No treatment for worm was given, because the patient left the hospital the day after the examination. A large number of eggs of *Ascaris* and occasional eggs of hookworm and *Trichuris* were found.

*Case 5.*—We could not secure authority to publish the clinical record of this case.

#### THE ANATOMY

*Historical.*—*Echinostoma ilocanum* was first discovered by Philip E. Garrison in Ilocano prisoners in Bilibid Prison, Manila, in 1908. He found the eggs in 5 cases and on treating his last case with male fern recovered 21 worms from the stools. He described the worms as a new genus and species, giving them the name *Fascioletta ilocana*. Later he sent 4 specimens to Doctor Odhner, at Upsala, and in a paper in the *Zoologischer Anzeiger*, in 1911, Doctor Odhner pointed out several new features of the anatomy and showed that the worms belong to the old genus *Echinostoma* whose type species is *Echinostoma echinatum* (Zeider 1903) found in domestic ducks and geese. Since that time there are no reports of the finding of this worm, although Willets reports finding similar eggs in one case in Cagayan.

Another species, *Echinostoma malayanum*, was reported in 1912 by Leiper from natives of Singapore and the Federated Malay States.

*Dimensions.*—In fifteen specimens measured Garrison found a maximum length of 6 millimeters and a maximum breadth of 1 millimeter and a minimum of 4 millimeters by 0.75 millimeter. We have found a somewhat greater range in the size of our specimens. The dimensions of eight worms, the first three collected on November 2 and the others on January 22, were as follows:

TABLE I.—Dimensions of 8 worms.

	Length. mm.	Maximum breadth. mm.
No. 1	4.03	0.98
No. 2	4.58	1.15
No. 3	4.80	1.34
No. 4	4.36	1.39
No. 5	5.16	1.83
No. 6	5.82	1.53
No. 7	6.46	1.46
No. 8	7.82	1.60

The greatest width of the body is at the level of the ventral sucker, from which point the body tapers gradually to the rounded posterior end. In front of the sucker is the head region, which is generally bent dorsally at the level of the genital pores; there is often a distinct constriction at this point. The shape and length of the head region vary considerably in different specimens due to the difference in the state of contraction of the worms. At the ventral sucker the body is almost round in cross section, but it becomes flattened rapidly toward each extremity.

*Color.*—There is very little pigment in the body wall. The fresh specimens were a transparent gray, and the testes, ovary, and uterine coils could be seen distinctly through the walls.

*Cuticular spines.*—Garrison says "the cuticle is smooth and without spines." Odhner describes a well-developed armor of scalelike spines which he says covers the anterior part of the body and is perceptibly developed on the margins of the body as far back as the border of the posterior testicle. We find in our specimens a very remarkable variation in regard to this feature of the body. In a few specimens the anterior part of the body was fairly well covered with very small spines, but in a majority of cases these spines are entirely lacking or are found only in irregular patches along the margins of the body. They are very unstable, and the least handling causes them to be lost. The cuticle of two of our best preserved specimens is smooth and shows no indications, even under a magnification of 400 diameters, of ever having borne spines at any time. It may be that the spines are developed and lost very early in the life of some worms, or some may fail entirely to develop spines at any time. When present they are so small that it is impossible to see how they could be of any use to the worms.

*Oral spines.*—Another variable feature of the anatomy is the presence or absence of the wreath of oral spines around the

mouth and anterior sucker, which is the most important characteristic of the genus *Echinostoma*. Garrison failed to note these spines in any of the specimens which he studied, and Odhner says of the four specimens sent him by Garrison that "the arrangement of the spines can only be followed in one specimen." From our 16 specimens we obtained only 3 in which any traces of these spines could be seen, and in only one specimen were they in a condition such that their arrangement could be studied. It seems that these spines, although much larger, are even more unstable than those of the cuticle (Plate I, fig. 1).

In the specimen described by Odhner 49 spines were present, which were arranged in the form of a wreath around the oral

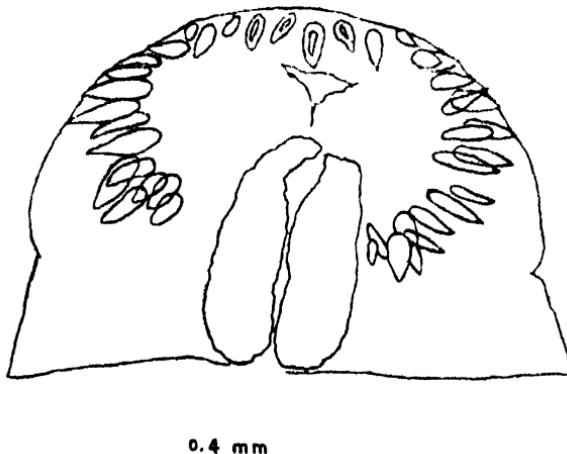


FIG. 1. Outline drawing of anterior end of *Echinostoma doceatum* (Garrison), showing the arrangement of the oral wreath of spines.

sucker, broken on the ventral side. There were two corner groups next to the ventral opening of 5 and 6 spines, respectively, then 2 single spines on each side, followed by 10 spines arranged in pairs, and finally 14 single spines forming the dorsal part of the wreath. The arrangement of the wreath in our specimen may be seen in fig. 1. As will be seen, there are only 39 spines present, but their arrangement is very much the same as described by Odhner. There are the two corner groups, the single spines, then the paired spines, and the row of dorsal spines. From a study of their arrangement it can be seen that several spines on our specimen have been lost.

The size of the spines in different parts of the wreath varies considerably. The largest ones in the corner groups are 50 mi-

crons long by 10 microns wide at the base. Then there is another type of a shorter, thicker form, 44 by 18 microns, and still smaller forms found in the corner groups and in the dorsal row, which average about 29 by 15 microns.

In those specimens where this wreath is not present no indication of such a structure can be seen, so it is not surprising that it was overlooked by Garrison. A drawing of a specimen without the spines is shown in Plate I, fig. 2.

*Ventral sucker*.—The ventral sucker is the most prominent feature of the surface of the body, the average size of this organ in 6 specimens being 530 microns in diameter. The center of the sucker lies at about the middle of the anterior third of the body.

*Alimentary tract*.—The oral sucker measures 120 to 200 microns in diameter and is slightly subterminal in position. It opens into a short prepharynx. The pharynx is globular in contracted specimens and has an average diameter of about 160 microns. In those specimens in which the head region is extended, the pharynx is considerably longer and decreases slightly in transverse diameter. The oesophagus is short (50 to 120 microns); it bifurcates just in front of the genital pores. The two unbranched intestinal cæca pass transversely outward to near the margins and then run posteriorly almost to the end of the body in the marginal region. In the posterior part of the body they are almost surrounded by the vitelline glands.

*Excretory system*.—The excretory pore is in the middle of the posterior border and opens into a large median excretory tube which runs forward to the posterior border of the posterior testicle, where it divides into two branches which run forward between the intestinal cæca and the reproductive organs. Thus they divide the body into three distinct regions, two lateral ones which contain the intestinal cæca and the vitelline glands and a median region containing the genital organs. In the region of the ventral sucker the tubes increase in diameter and appear to unite dorsad to the sucker.

*Male genital organs*.—The testes lie in the posterior half of the middle region of the body, one behind the other. In some specimens they are oval and appear as solid masses, but generally they are elongated and are distinctly divided into anterior and posterior lobes by a transverse constriction. From each testicle a vas deferens runs forward near the margin of the genital region. They unite dorsad to the posterior sucker and enter the posterior end of the cirrus pouch. The opening of the cirrus

pouch lies just back of the bifurcation of the intestine and in front of the ventral sucker, and the pouch extends back dorsad to the sucker, being about twice as long as it is wide. In its posterior part is a seminal vesicle, into which the vasa deferentia open. It is capable of considerable distention, so that in some cases it nearly fills the cirrus pouch, while in others it seems to be very small. It opens directly into a muscular cirrus, which is long and spirally coiled and often is extended through the genital pore.

*Female genital organs.*—The ovary is globular and is situated a little to the right of the median line at about the middle of the length of the body. Its oviduct passes into a rounded "shell gland," which lies between the ovary and the anterior testicle in the middle line of the body. The vitelline glands commence about midway between the posterior border of the ventral sucker and the anterior border of the ovary. They extend to the posterior end of the body. In the anterior part they lie entirely in the lateral margin, but as they pass back, they spread out dorsally and ventrally and almost completely surround the body posterior to the testes. The transverse vitelline ducts turn inward just anterior to the testes and enter the shell gland posterolaterally. A receptaculum seminis is not present. The uterus leaves the shell gland on the left side and turns anteriorly to in front of the ovary, where the coils begin. They fill all of the space in the middle region of the body between the ovary and the ventral sucker. The anterior part of the uterus forms a well-developed vagina, which passes forward dorsad to the ventral sucker and opens at the female genital pore, which lies just to the left of the male pore.

*Ova.*—The ova have been well described by Garrison in his paper. They have a thin shell with an operculum at the smaller end and are not segmented when passed in the faeces. The variation in length and breadth is considerable, but from a measurement of 25 fresh eggs, we get nearly the same average size as Garrison. His measurements are:

Maximum length, 114.7; breadth, 81.9 microns.

Minimum length, 88.8; breadth, 53.5 microns.

Average length, 99.58; breadth, 56.04 microns.

Our measurements are:

Maximum length, 111; breadth, 74.4 microns.

Minimum length, 88.8; breadth, 53.6 microns.

Average length, 101.21; breadth, 56.4 microns.

## LITERATURE

- GARRISON, PHILIP E. A new intestinal trematode of man. *Phil. Journ. Sci., Sec. B* (1908), 3, 385-392.
- ODHNER, T. *Echinostomum ilocanum* (Garrison 1908), ein neuer Menschen-parasit aus Ostasien. *Zool. Anz.* (1911), 38, 65-68.



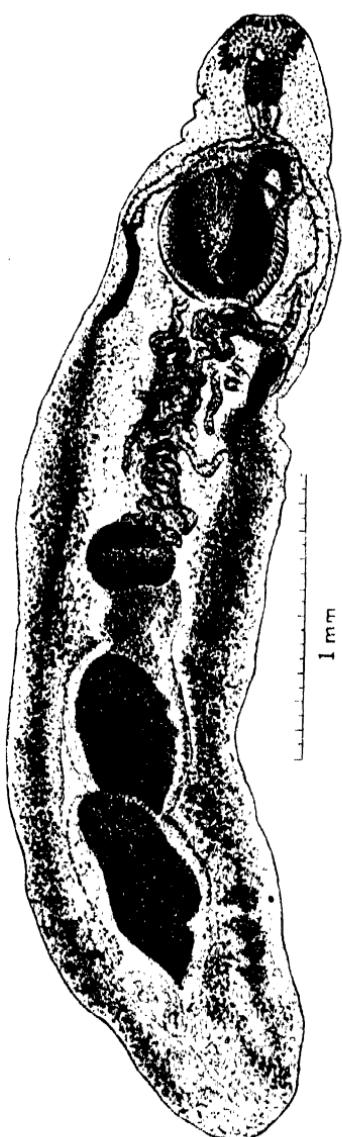


Fig. 1.

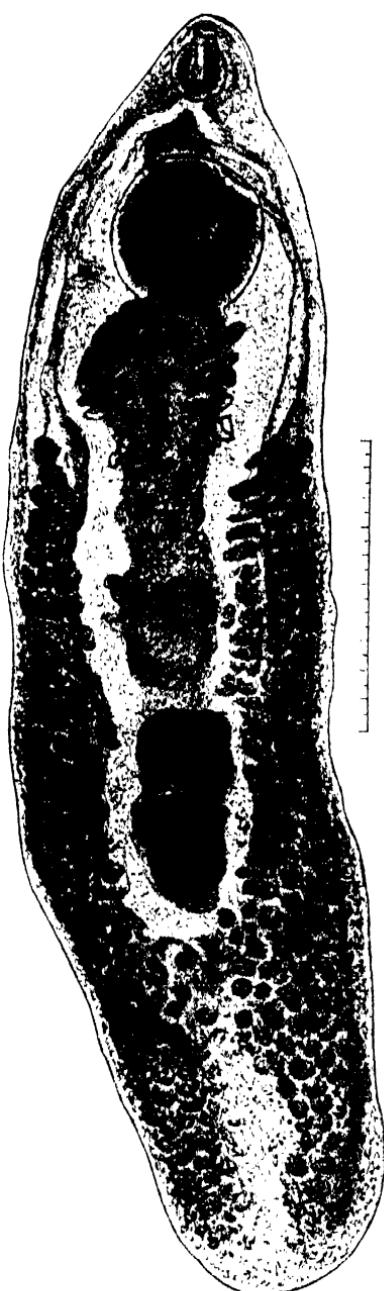


Fig. 2.



THE PHILIPPINE  
JOURNAL OF SCIENCE  
B. TROPICAL MEDICINE

VOL. XII

SEPTEMBER, 1917

NO. 5

A SURVEY OF CERTAIN CHEMICALS WITH REGARD TO THEIR  
BACTERICIDAL ACTION ON CHOLERA VIBRIOS WITHIN  
THE BODY OF EXPERIMENTAL CHOLERA CARRIERS<sup>1</sup>

By OTTO SCHÖBL

(From the Serum Section of the Biological Laboratory, Bureau of Science,  
Manila, and the Quarantine Laboratory, Health Officers'  
Department, Port of New York)

An experimental study of the bactericidal action of drugs upon cholera vibrios in the animal body is of considerable interest. It presents a rational method of searching for a remedy for the cure of cholera carriers and offers a method of testing the value of the so-called intestinal antiseptics.

Previously published studies on experimental cholera carriers brought to light the following facts. Direct inoculation of cholera culture into the gall bladder is the safest method of producing the state of cholera carriers in experimental animals.(1) A comparatively small amount of cholera culture, injected into the gall bladder, may suffice to produce this condition in animals.(2) The virulence of the cholera culture increases by being passed from one carrier to another.(3) The condition in question is an inflammation,(4) more or less pronounced, of the gall bladder, which under certain circumstances may extend to the liver. No evidence was found to indicate that the infection would extend further so as to assume the septicæmic type. Once the cholera vibrios establish themselves in the gall passages, the bile offering favorable conditions, they multiply therein and are being discharged into the small intestine, where they remain practically without competition. In the large intestine, due to the presence of numerous other bacteria, the

<sup>1</sup> Received for publication May 26, 1917.

cholera vibrios are not found as regularly as they are in the proximal part of the intestine. They are rarely excreted in the faeces, unless the sojourn of the intestinal contents is hastened through the large intestine and the conditions are made favorable to the survival of the cholera vibrios.(4, 5)

From these findings it is evident at once that the problem of drug treatment in experimental cholera carriers is one of great difficulty. Even a drug which, given by mouth, would exert bactericidal action upon the cholera vibrios in the intestine would not bring about a complete and permanent disappearance of cholera vibrios from the body organism unless it was eliminated through the bile in such a chemical form as to be toxic to the cholera vibrios in a higher degree than it is deleterious to the body organism.

Guinea pigs were selected for these experiments for several reasons. It has been found and already mentioned in a previous paper that the inflammation of the gall bladder, following the intravesicular injection of cholera culture, is far more intense in rabbits than in guinea pigs.(3) It was to be expected, therefore, that the effect of a drug would be evident in case of a slight infection, more so than in a case of a severe one. Furthermore, in previous experiments on six rabbits, which were found positive in from three to thirteen days after the infection, four harbored the cholera vibrios in the gall bladder only(3) and not in the intestine. Should rabbits be used for treatment experiments, it would be difficult at times to say whether or not the disappearance of cholera vibrios from the intestine, in itself a therapeutic result of value, is due to the action of the drug. Besides these considerations it was found technically more convenient and more economic to use guinea pigs.

#### THE ARRANGEMENT OF EXPERIMENTS

*Infection.*—The intravesicular injection was used exclusively in these experiments. A recently isolated culture of cholera was grown in ox bile and transplanted in agar twenty-four hours before the injection was performed. The animals were shaved, and the skin was washed with lysol solution and then painted with tincture of iodine. In performing the operation, an incision was made from the middle of the xiphoid process to the right costal margin. As soon as the muscles were separated, the peritoneum became visible and through it the xiphoid process. The latter was clasped with a hemostat and lifted up, whereupon the duplicature of the peritoneum formed thereby was perforated by means of a dull forceps. As a rule, the gall bladder was

immediately visible, and prolapsing into the laparotomy wound, it closed the opening, thus preventing exposure of the other organs. Therefore the injection could be made outside the peritoneal cavity. Only fractions of a cubic centimeter were injected into the gall bladder. The inoculation finished, the puncture in the gall bladder was closed with a ligature, the ends of the wound were lifted up, and the gall bladder assumed its normal position. Threads thoroughly soaked with tincture of iodine were used for suturing the abdominal wound.

*Examination.*—To ascertain the effect of the drug, the animals were killed and examined within several hours after the last administration of the drug. The shaved skin over the chest and abdomen was wetted with 2 per cent lysol solution. The abdomen and thorax were opened separately. The gall bladder, the proximal part of the intestine (in the reports, duodenum), the distal part of the small intestine (in the reports, the ileum), and the cæcum were removed from the abdomen—first the gall bladder, then the duodenum, ileum, cæcum, in order, a separate set of sterilized instruments being used for each organ. The gall bladder was taken out in toto, including a portion of the bile duct. The contents of the gall bladder were emptied into peptone water, and the gall bladder, together with the bile duct, was placed in a culture tube. The contents of the proximal part of the small gut were planted, and the intestine, cut into small pieces, was added to the same peptone tube. At least one half of the distal part of the small intestine was planted in the same way as the duodenum. Five large loopfuls of the contents of the cæcum were inoculated into peptone water. One loopful of the contents of the various organs mentioned above was plated directly on Dieudonné agar plates. After six hours of incubation second peptone cultures were planted from the first peptone tubes. At the end of twenty-four hours Dieudonné plates were made from the first and the second peptone cultures.

It was the purpose of these experiments to test as many chemicals as possible in the hope that some of them would show an indication of curative effect. For this reason comparatively few animals were treated with each drug, the intention being to extend the experiments later on, using those chemicals which showed promising results in the present investigations.

As to the dosage of the drugs small doses were given at the start. The quantity of the drug was gradually increased until toxic symptoms—even death—occurred as a consequence of the drug feeding. It was intended to saturate the body organism of the animals with the particular drug. In order to see the imme-

diate effect of the drug upon the cholera vibrios, particularly in the intestine, the animals were killed within a few hours after the last feeding instead of awaiting the time when a complete elimination of the chemical from the animal body could be reasonably expected.

The objection to such a procedure, namely, the possibility of transferring into the culture medium an amount of the drug sufficient to inhibit the growth of cholera vibrios in the cultures, was kept in mind, but it soon became evident that this factor hardly warranted consideration. Numerous experiments with various chemicals were made in this way without any apparent curative effect of the drugs being noticeable. Furthermore the present investigation was intended for orientation only, and those drugs which showed any effect at all were to be further studied.

The results of our experiments are summarized in Tables I to VIII. From ten to twelve animals were inoculated and treated at the same time, one of the carriers, at least, being kept as a control. The administration of the drugs took place either by intramuscular injection or by mouth. For the latter way of drug application an inert oil was found technically more convenient than water. The animals under treatment were killed not later than the tenth day, provided they survived the treatment that long. It has been found in our previous experiments that a certain percentage of experimental cholera carriers become spontaneously negative after the thirteenth day. Therefore the duration of treatment had to be limited to ten days.

For the sake of convenience we have arranged the chemicals and drugs that were used in the present experiments into seven groups.

The first group contains simple organic compounds: Benzene, toluene, and xylene.

The second group contains halogen derivatives: Chloroform, bromoform, and chloral.

The third group represents phenols and related compounds: Salicylates, benzoic acid, resorcin, brenzkatechin, guaiacol, gallic acid, pyrogallol, carvacrol, thymol, creosote, xylenol, and alpha- and beta-naphthol.

The fourth group contains miscellaneous organic compounds, the majority of which are official in the pharmacopœia: Urotropin, Ol. caryophylli, Ol. cinamoni, Ol. copaibæ, camphor, eucalyptol, anethol, phenetol, terpineol, and turpentine.

Two alkaloids, namely, quinine and emetine, were tried also because of their usefulness in chemotherapy. (The fifth group.)

Certain representatives of the officinal compounds of metals

were placed in the sixth group. Magnesium peroxide, potassium iodide, potassium permanganate, calomel, mercury salicylate, antimony tartrate, antimony trioxide, arsenic trioxide, sodium cadoxylate, atoxyl, 606 Ehrlich.

The seventh group comprises a few anilin dyes. It is known of some of these chemicals that they act *in vitro* as strong and selective antiseptics. The following dyes were tested: Methylene blue, gentian violet, brilliant green, fuchsin, trypan red and blue, scarlet red, chrysoidin, vesuvin, victoria blue, and crystal violet.

Judging the effect of drug treatment by the results of these experiments, one can see that none of the drugs tested showed such prompt effect as to bring complete sterilization of the animal's body organism in a short time in every case.

Nevertheless there are certain indications evident of the possibility of shortening the duration of the state of cholera carrier. The effect of drug treatment in our experiments appears to be of three degrees.

*First degree.*—The absence of cholera vibrios on the direct plates made from the intestine, indicating diminution of cholera vibrios in the intestinal tract. Findings of this type are considered of little importance, since physiologic conditions undoubtedly influence the variation in numbers of cholera vibrios in the intestine. Nevertheless, compared with the findings in untreated controls, the absence of cholera colonies on direct plates can be considered as an effect of drug treatment, and drugs effecting such findings deserve further attention.

*Second degree.*—Absence of cholera vibrios on direct plates as well as in peptone cultures both made from the intestine, indicating absence of cholera vibrios from the intestine at that time. Drugs showing this effect may reasonably be considered intestinal antiseptics of value, in as much as they bring about a disinfection of the intestine even if only temporarily.

*Third degree.*—Absence of cholera on all direct plates and in all peptone cultures, including those made from bile and from the gall bladder. Considering the ease with which cholera vibrios can be detected with the aid of a selective medium and particularly by employing the peptone enrichment process, one is bound to consider these findings as sufficient evidence of complete absence of cholera vibrios from the body organism.

In this group (Table I) only benzene showed a slight effect in as much as one out of three guinea pigs after ten days' treatment harbored so few cholera vibrios in the intestine that none grew on direct plates. Cholera vibrios, however, were detected by the enrichment process.

No curative effect was noticeable in these experiments (Table II). The majority of animals died as a consequence of the treatment. Autopsy revealed extensive degeneration of the internal organs, particularly of the liver.

The following chemicals showed an indication of curative effect (Table III) :

1. Brenzkatechin. One animal treated with this chemical for nine days showed no cholera on direct plates, but cholera vibrios were present in peptone cultures.

2. Guaiacol. In three of four animals treated with guaiacol there was an effect noticeable. Twice cholera vibros were not found at all in the ileum, while in one case after nine days' treatment the cholera vibrios were absent from the entire alimentary tract.

3. Pyrogalol. First degree effect after nine days' treatment.

4. Carvacrol. Second degree effect in one animal treated eight days, no effect in one animal treated seven days. Both animals died.

In this group (Table IV) only turpentine showed a slight effect of the first degree, but the animal died in two days.

The following chemicals of this group showed an indication of a curative effect (Table VI) :

1. Antimony trioxide. Curative effect of first degree in one animal after eight days' treatment. In another animal no effect was noticeable after four days' treatment.

2. Arsenic trioxide. This chemical, given in large doses, brought about death in two animals treated; in small doses after nine days' treatment by intramuscular injections, complete disappearance of cholera vibrios from the entire alimentary canal. Application by mouth of the same chemical for three days remained without effect in one case.

3. Atoxyl and sodium cacodylate showed effect of first degree after eight and nine days' treatment, respectively.

4. Ehrlich-Hata 606. Twelve experimental cholera carriers were treated by intramuscular injections of this drug. Four of them died. In four of the twelve the cholera vibrios have apparently disappeared completely during the treatment; in the other two the effect of the first degree was noticeable.

Of the dyes tested in these experiments (Table VII) only methylene blue deserves mention. It showed a first degree effect in one instance.

These experiments are by no means final; still they show that the problem of drug treatment of cholera carriers is not utterly hopeless. None of the chemicals gave such prompt curative effect as to bring about complete disappearance of cholera vibrios from the animal's body in every case. It is hardly probable that any such drug will be found. The drugs listed as phenol group and the arsenic compounds are of some promise. Since it is within our power to prolong the duration of the carrier state in animals by feeding bile,(5) it is hoped that drug-treatment experiments performed on bile-fed animals will allow a period of treatment extended beyond the ten days' limit and thus bring more definite results than those obtained in the present investigations. Combination treatment by several drugs suggests itself also.

#### REFERENCES

1. *Journ. Inf. Dis.* (1916), 18, 307-314.
2. *Phil. Journ. Sci., Sec. B* (1916), 11, 153-155.
3. *Journ. Inf. Dis.* (1916), 19, 145-152.
4. *Phil. Journ. Sci., Sec. B* (1916), 11, 157-158.
5. *Ibid., Sec. B* (1917), 12, 23.

TABLE I.—*Showing the results of experiments with benzene, toluene, and xylene.*  
 [—, cholera vibrios not found; +, cholera vibrios present; v. n., more than 200; f., about 200; t., less than 6; o., not examined;  
 p. o., per os; int., intramuscular; inj., injection.]

Animal No.	Drug.	Duration.	Total amount administered, drug.	Autopsies, days after infection.				Direct plates.				Peptone cultures.			
				Sick.	Well.	Bile.	Duo-denum.	Ileum.	Cæcum.	Gall-bladder.	Duo-denum.	Ileum.	Cæcum.	Cæcum.	
1..... Benzene.....	8	1.50	p. o.	Yes.....	No.....	10	v. n.	—	v. f.	v. f.	—	+	+	+	+
2..... do.....	8	1.50	p. o.	Yes.....	No.....	10	f.	v. f.	v. f.	v. f.	—	+	+	+	+
3..... do.....	10	3.25	p. o.	Yes.....	No.....	10	f.	—	—	—	—	+	+	+	+
1..... Toluene.....	4	1.85	p. o.	Yes.....	No.....	5	o.	o.	o.	o.	+	+	+	+	+
2..... do.....	5	1.06	p. o.	Yes.....	No.....	6	v. n.	f.	v. f.	v. f.	—	+	+	+	+
3..... do.....	8	1.50	p. o.	Yes.....	No.....	10	n.	f.	f.	m.	+	+	+	+	+
1..... Xylene.....	3	1.60	p. o.	Yes.....	No.....	4	v. n.	n.	v. n.	f.	+	+	+	+	+
2..... do.....	5	1.06	p. o.	Yes.....	No.....	6	v. n.	f.	n.	v. f.	+	+	+	+	+
3..... do.....	8	1.50	p. o.	Yes.....	No.....	10	v. n.	v. f.	v. f.	—	+	+	+	+	+

TABLE II.—*Showing the results of experiments with chloroform, bromoform, and chloral.*

[See Table I for abbreviations and signs.]

Animal No.	Drug.	Duration.	Total amount of drug.	Administered.	Sick.	Well.	Direct plates.				Peptone cultures.			
							Days.	σ.	Bile.	Duo-denum.	Gall-bladder.	Duo-denum.	Ileum.	Cæcum.
1. Chloroform	do	2.00	p.o.	Yes	No	v.n.	3	v.n.	v.n.	v.n.	+	+	+	+
2. do	do	0.30	p.o.	Yes	No	v.n.	4	n.	—	n.	+	+	—	+
3. do	do	0.30	p.o.	Yes	No	v.n.	4	v.n.	v.n.	v.n.	f.	+	—	+
4. do	do	0.30	p.o.	Yes	No	v.n.	6	o.	o.	o.	f.	+	+	—
1. Bromoform	do	0.10	p.o.	Yes	No	v.n.	4	v.n.	v.n.	v.n.	—	+	+	—
2. do	do	0.15	p.o.	Yes	No	v.n.	6	v.n.	v.n.	v.n.	—	+	—	+
1. Chloral	do	0.34	p.o.	Yes	No	v.n.	7	v.n.	v.n.	v.n.	n.	+	+	+
2. do	do	0.34	p.o.	Yes	No	v.n.	7	v.n.	v.n.	v.n.	n.	+	+	+

TABLE III.—*Showing the results of experiments with phenols and closely related compounds.*

[See Table I for abbreviations and signs.]

Animal No.	Drug.	Duration.	Total amount administered of drug.	Sick.	Well.	Autopst. days after infection.	Direct plates.			Peptone cultures.				
							Bile.	Duo-denum.	Ileum.	Gall-bladder.	Duo-denum.	Ileum.	Cecum.	
1.	Sodium salicylate.	Dose. g.	0.60	P.o.	Yes	No.	2	o.	o.	d.	d.	+	+	+
2.	do	7	0.80	P.o.	No	Yes	8	f.	f.	t.	t.	+	+	+
1.	Salol.	8	0.15	P.o.	No	Yes	13	o.	o.	o.	o.	+	+	+
2.	do	9	1.60	P.o.	No	Yes	9	n.	f.	t.	t.	+	+	+
1.	Methyl salicylate.	3	1.50	P.o.	Yes	No.	5	o.	o.	d.	d.	+	+	+
1.	Saliprin.	6	1.50	P.o.	No	Yes	7	v.n.	v.f.	n.	f.	+	+	+
1.	Benzolic acid.	10	1.50	P.o.	No	Yes	10	n.	v.f.	f.	v.f.	+	+	+
1.	Resorcin.	8	0.62	P.o.	No	Yes	9	n.	n.	n.	n.	+	+	+
1.	Brenkatechin.	8	0.30	P.o.	Yes	No.	4	v.n.	v.n.	v.n.	v.n.	+	+	+
2.	do	9	0.30	P.o.	Yes	No.	10	f.	—	—	—	+	+	+
1.	Guaiacol.	6	0.06	P.o.	No	Yes	7	f.	v.f.	—	—	+	+	+
2.	do	7	1.13	P.o.	Yes	No.	7	v.n.	v.n.	—	—	+	+	+
3.	do	9	1.60	P.o.	Yes	No.	10	—	—	—	—	+	+	+
4.	do	10	2.13	P.o.	Yes	No.	10	f.	v.f.	—	—	+	+	+
1.	Gallic acid.	8	0.5	P.o.	Yes	No.	9	v.n.	f.	n.	d.	+	+	+
1.	Pyrogalol.	8	0.6	P.o.	Yes	No.	9	f.	—	—	—	+	+	+
1.	Carvacrol.	7	1.07	P.o.	Yes	No.	7	v.	f.	n.	—	+	+	+
2.	do	8	1.07	P.o.	Yes	No.	8	—	—	—	—	+	+	+
1.	Thymol.	8	0.076	P.o.	No	Yes	13	o.	o.	d.	d.	+	+	+
2.	do	3	0.30	P.o.	Yes	No.	6	o.	o.	d.	d.	+	+	+
3.	do	7	0.70	P.o.	Yes	No.	9	v.n.	f.	v.f.	—	+	+	+
1.	Cresote.	4	0.04	P.o.	Yes	No.	6	n.	n.	v.n.	f.	+	+	+
1.	Cresonal.	8	1.20	P.o.	Yes	No.	10	v.n.	n.	v.n.	v.n.	+	+	+
1.	Xylool.	6	0.96	P.o.	Yes	No.	6	v.n.	v.n.	v.n.	v.n.	+	+	+

2	do	8	1.16	p.o.	Yes	No	9	v.n.	v.r.	v.n.	v.n.	v.n.	v.n.	v.n.
1	Alphanaphthol	4	0.2	p.o.	Yes	No	7	n.	n.	n.	f.	f.	f.	f.
1	Betanaphthol	3	0.30	p.o.	Yes	No	6	a.	a.	a.	o.	o.	o.	o.
2	do	8	0.35	p.o.	No	Yes	9	v.n.	v.f.	v.f.	-	-	-	-
8	Betol	2	0.2	p.o.	Yes	No	3	a.	a.	a.	o.	o.	o.	o.
4	do	3	0.3	p.o.	Yes	No	6	a.	a.	a.	o.	o.	o.	o.

TABLE IV.—*Showing results of experiments with miscellaneous organic compounds.*

[See Table I for abbreviations and signs.]

Animal No.	Drug.	Duration.	Total amount of drug.	Sick.	Well.	Autopsy, days after infection.	Direct plates.			Peptone cultures.			
							Bile.	Duodenum.	Ileum.	Gall-bladder.	Duodenum.	Ileum.	Cecum.
1. Urotropin		Days.	g.	No.	Yes	6	o.	o.	o.	o.	+	+	+
2. do		3	1.25	p.o.	Yes	8	o.	o.	o.	o.	+	+	+
2. do		6	2.00	p.o.	Yes	9	v.n.	n.	v.n.	v.n.	+	+	+
3. do		8	9.00	p.o.	Yes	9	v.n.	n.	v.n.	v.n.	+	+	+
1. Oleum caryophylli		4	0.57	p.o.	No.	4	v.n.	v.n.	v.n.	v.f.	+	+	+
2. do		10	1.67	p.o.	No.	10	v.n.	n.	v.n.	v.n.	+	+	+
1. Oleum cinnamoni		5	0.59	p.o.	Yes	7	v.n.	f.	v.n.	v.n.	+	+	+
1. Oleum copalae		1	0.20	p.o.	Yes	3	o.	o.	o.	o.	+	+	+
2. do		3	1.50	p.o.	Yes	4	o.	o.	o.	o.	+	+	+
1. Camphor		3	0.30	p.o.	Yes	5	o.	o.	o.	o.	+	+	+
2. do		3	0.30	p.o.	No.	4	n.	f.	v.n.	v.n.	+	+	+
1. Eucalyptol		5	1.40	p.o.	Yes	10	o.	o.	o.	o.	+	+	+
1. Anethol		5	0.50	p.o.	No.	6	v.n.	v.n.	v.n.	v.n.	+	+	+
2. do		10	2.48	p.o.	No.	10	v.n.	f.	n.	v.n.	+	+	+
1. Phenethol		9	3.13	p.o.	Yes	9	v.n.	v.n.	v.n.	v.n.	+	+	+
2. do		9	3.13	p.o.	No.	9	v.n.	v.n.	v.n.	v.n.	+	+	+
1. Terpineol		7	1.63	p.o.	Yes	7	v.n.	v.n.	v.n.	v.n.	+	+	+
2. do		9	2.63	p.o.	No.	9	v.n.	v.n.	v.n.	v.n.	+	+	+
1. Terpine		2	0.20	p.o.	Yes	3	f.	v.n.	v.n.	v.n.	+	+	+

TABLE V.—Showing the results of experiments with quinine and emetine.

[See Table I for abbreviations and signs.]

TABLE VI.—*Showing the results of experiments with inorganic compounds.*

[See Table I for abbreviations and signs.]

Animal No.	Drug.	Duration.	Total amount of drug.	Administered.	Sick.	Well.	Peptone cultures.			Direct plates.			Gall-blad-der.	Ca-eum.	
							Days.	g.	Autop-sy, days after infection.	Bile.	Duo-denum.	Bile.	Duo-denum.		
1.	Magnesium peroxide	4	8.00	D. o.	No.....	Yes.....	6	v. n.	n.	f.	+	+	+	+	+
2.	do	7	3.50	D. o.	No.....	Yes.....	9	v. n.	f.	n.	-	+	+	+	+
1.	Potassium iodide	1	0.50	D. o.	No.....	Yes.....	2	o.	o.	o.	+	+	+	+	+
2.	do	7	0.80	D. o.	No.....	Yes.....	8	v. n.	v. n.	v. n.	+	+	+	+	+
1.	Potassium permanganate	3	0.30	D. o.	No.....	Yes.....	17	o.	o.	o.	+	+	+	+	+
2.	do	8	0.30	D. o.	Yes.....	No.....	4	v. n.	n.	t.	-	+	+	+	+
1.	Calomel	1	0.10	D. o.	Yes.....	No.....	4	o.	o.	o.	+	+	+	+	+
2.	do	3	0.015	D. o.	Yes.....	No.....	4	v. n.	v. n.	n.	+	+	+	+	+
3.	do	6	0.045	D. o.	Yes.....	No.....	7	o.	o.	o.	+	+	+	+	+
1.	Mercury salicylate	3	0.02	D. o.	Yes.....	No.....	4	v. n.	v. n.	f.	+	+	+	+	+
2.	do	6	0.05	int.	No.....	Yes.....	8	o.	o.	o.	+	+	+	+	+
1.	Antimony tartarate	1	0.006	D. o.	Yes.....	No.....	2	n.	n.	f.	+	+	+	+	+
2.	do	1	0.006	p. o.	Yes.....	No.....	1	n.	n.	f.	+	+	+	+	+
3.	do	6	0.045	int.	No.....	Yes.....	6	n.	v. f.	n.	+	+	+	+	+
1.	Antimony trioxide	4	0.056	int.	No.....	Yes.....	6	v. n.	n.	v. n.	-	-	-	-	-
2.	do	8	0.056	int.	No.....	Yes.....	10	n.	-	-	-	-	-	-	-
1.	Arsenic trioxide	1	0.006	int.	Yes.....	No.....	2	n.	n.	f.	+	+	+	+	+
2.	do	1	0.006	int.	Yes.....	No.....	2	f.	f.	f.	+	+	+	+	+
3.	do	3	0.004	D. o.	No.....	Yes.....	6	n.	f.	f.	+	+	+	+	+
4.	do	9	0.0035	int.	No.....	Yes.....	10	-	-	-	-	-	-	-	-
1.	Sodium caecodylate	9	1.34	int.	No.....	Yes.....	10	v. f.	v. f.	v. f.	+	+	+	+	+
2.	do	8	1.34	int.	No.....	Yes.....	6	n.	n.	n.	+	+	+	+	+
1.	Amtryl	1	0.006	int.	Yes.....	No.....	6	n.	n.	n.	+	+	+	+	+
1.	Kirklich 605	2	0.020	int.	Yes.....	No.....	6	n.	n.	n.	+	+	+	+	+





TABLE VIII.—*Showing untreated controls.*

[See Table I for abbreviations and signs.]

Animal No.	Drug.	Autop-sy days after infec-tion.	Direct plates.				Peptone cultures.			
			Bile.	Duo-denum.	Ileum.	Cae-cum.	Gall-blad-der.	Duo-denum.	Ileum.	Cae-cum.
1.....	Control.....	4	n.	f.	n.	v. f.	+	+	+	+
2.....	do.....	5	v. n.	v. n.	n.	f.	+	+	+	+
3.....	do.....	6	v. n.	n.	v. n.	n.	+	+	+	+
4.....	do.....	6	v. n.	f.	n.	f.	+	+	+	+
5.....	do.....	6	v. n.	n.	n.	—	+	+	+	—
6.....	do.....	7	v. n.	v. n.	n.	v. f.	+	+	+	+
7.....	do.....	7	v. n.	f.	v. n.	v. f.	+	+	+	+
8.....	do.....	9	n.	v. f.	f.	—	+	+	+	+
9.....	do.....	10	v. n.	n.	f.	—	+	+	+	—
10.....	do.....	10	n.	—	f.	—	+	+	+	—
11.....	do.....	10	n.	—	n.	—	+	+	+	—
12.....	do.....	10	v. n.	n.	v. n.	n.	+	+	+	+
13.....	do.....	11	v. n.	f.	f.	—	+	+	+	+

150681—2



## INCIDENCE OF AGE, ATHEROMA, AND ANEURISMS AS SEEN IN AUTOPSIES OF FILIPINOS<sup>1</sup>

By C. H. MANLOVE

(From the Department of Pathology and Bacteriology, University of the Philippines)

This report is based on a study of the autopsy records from the department of pathology and bacteriology, of the University of the Philippines, and on statistics of the Philippine Health Service. The total number of records of autopsies examined is 5,400, which were performed over a period of nine years. The report is similar to one from India by Rogers.

### AGE INCIDENCE

An examination of Rogers's(5) work on age incidence in India shows his report to be as follows. The great majority of deaths occurs at an early period of life. In his autopsy series although but 2.7 per cent were under 11 years of age, yet 80 per cent of the Hindus and 62 per cent of the Mohammedans were not above 40 years of age, while 52 per cent of the Hindus and 44 per cent of the Mohammedans were not over 30 years of age. Further, only 6 per cent were from 51 to 60 years of age. He also states that these early deaths cannot be fully accounted for by the prevalence of tropical diseases, such as cholera, dysentery, and tropical fevers.

The Philippines, as India, has a high mortality at an early period of life. During 1914, out of a population of 6,925,319 people within the registration area, we find that 55.49 per cent of all deaths occurred between the ages of 0 and 9 years, 72.91 per cent before the age of 40 years, 6.18 per cent between the ages of 40 and 49 years, 5.26 per cent between 50 and 59 years, and 14.96 per cent above 60 years of age. In 0.50 per cent the age is not stated.

The age incidence in Manila, as found by examination of the records of 2,000 consecutive autopsies, shows 36.7 per cent of all deaths to occur before the age of 10 years, 81.05 per cent before the age of 40 years, 8.1 per cent between the ages of 41 and 50 years, and 10.85 per cent above 50 years of age, the average age

<sup>1</sup> Received for publication July, 1917.

at death being 22.98 years, and the average age at death occurring after 11 years being 35.25 years.

When interpreting the high mortality which occurs so early in life, the following must be considered: High infant mortality, tuberculosis, and the tropical diseases, such as cholera, dysenteries, and tropical fevers. During one year the average death rate of Filipino infants less than 1 year of age was 486.77 per 1,000, which is a mortality of almost 50 per cent.

Tuberculosis causes a large number of deaths in all decades. It has been the cause of death in 8 per cent of all infants up to 5 years of age which have come to autopsy in Manila.(4)

The United States Census Bureau calculated in 1912 that 400,000 of the present inhabitants of the Philippine Islands were doomed to die of tuberculosis.

The prevalence of cholera, the dysenteries, tuberculosis, and other diseases in the Philippines are shown in Table I, compiled from the Philippine health statistics.

TABLE I.—*General causes of death and number of deaths in the Philippines during 1914.*

Tuberculosis	18,009
Fevers	22,102
Cholera	2,018
Dysenteries and diarrhoeas	12,381
Other infectious diseases	6,048
Beriberi	4,040
Convulsions of infants under 5 years of age	22,057
Leprosy	21
Violence	1,834
Cerebral hemorrhage	581
All other causes	65,938
Total number of deaths	155,029

#### ATHEROMA

A study of the presence and extent of atheroma with associated cardiac and renal changes in Filipinos was made to determine the possibilities which these changes might have in explaining the cause of death after the age of 40 years.

An examination of Table I shows that only about 58 per cent of all deaths can be accounted for by tuberculosis, infantile convulsions, and the more typical tropical diseases. Thus there are about 42 per cent in which the cause of death has not been specifically recorded. It is safe to say that among this 42 per cent of nonspecifically recorded deaths there is a large percentage of those who live beyond the age of 40 years, as the majority of deaths from the diseases recorded in Table I occurs before the age of 40 years. Also it may be stated that in this 42 per cent

is the majority of those deaths influenced by arterial, cardiac, or renal changes.

TABLE II.—*Percentage of slight and marked atheroma among natives of India in different decades. (5)*

Age in years.	Normal.	Slight.	Marked.	Granular kidney in atheroma cases.
Up to 10	100	0.0	0.0	0.0
11 to 20	93.8	6.7	0.0	0.0
21 to 30	81.3	16.2	2.5	9.8
31 to 40	70.1	24.2	5.7	16.8
41 to 50	52.6	28.0	19.4	16.4
51 to 60	40.6	24.8	34.8	26.8
Over 60	38.1	38.8	28.6	69.2
Up to 40	79.4	18.4	2.2	18.1
Over 40	47.5	27.4	25.1	26.1
Total	72.6	19.4	8.0	18.5

TABLE III.—*Sex and race incidence of atheroma. (5)*

	Males.	Females.	Hindus.	Mohammedans.
Slight atheroma	21.4	13.0	19.5	19.5
Marked atheroma	7.4	9.2	7.3	9.75
Total	28.8	22.2	26.8	29.25
Up to 40 years	22.2	18.8	20.2	21.1
Over 40 years	52.0	57.5	52.5	50.9

Rogers has stated that in India the early deaths cannot be fully accounted for by the prevalence of tropical diseases. This led him to make a study of the arteries, with a view to determining the degree of atheromatous changes which had taken place in the arteries during the different decades. He notes, as the most important point brought out by the analysis, the sudden and great increase of marked arterial degeneration as soon as the age of 40 years is passed. The sex incidence shows only a slight preponderance in males. However, the lesser incidence in Indian females is confined to the slighter degrees of arterial degeneration and to below the age of 41 years, both the more marked degrees of atheroma and the incidence over 40 years of age being actually higher in the females than in the males. The average age of all females in his series is lower than that of the males, 17.7 per cent of the women having been over 40 years of age at the time of death. This is in accordance with the greater frequency of marked atheroma among the females as compared

TABLE IV.—Percentage of atheroma cases with hypertrophy of heart and chronic interstitial nephritis in different decades of 1,000 Filipinos.

		Sexes and total.		Ages in decades.			
		0 to 10		11 to 20		21 to 30	
		Males		Females		Males	
		Number of cases examined.	Normal arteries.	Slight atherosclerosis.	Marked atherosclerosis.	Hyper-trophy of heart in cases of atherosclerosis.	Absence of hypertrophy of heart in cases of atherosclerosis.
		54	54	54	54	54	54
0 to 10		29	29	100	100	0	0
Total							
Males		127	88.19	11.81	0.0	6.66	32.34
Females		50	88.00	10.0	2.0	33.33	66.66
Total		177	88.14	11.3	0.66	14.28	55.72
Males		159	81.13	17.07	1.89	6.66	32.34
Females		89	80.89	13.48	5.62	17.55	52.44
Total		248	81.06	15.72	3.22	10.64	50.96
Males		123	73.17	15.44	11.38	50.00	40.00
Females		56	61.81	23.63	14.54	33.83	66.66
Total		178	69.66	17.97	12.37	43.14	55.96
Males		108	88.88	25.00	36.11	43.33	55.07
Females		36	36.11	22.22	41.66	25.09	73.91
Total		144	38.2	24.3	37.5	39.32	60.68
Males		121	21.49	13.22	65.29	45.45	54.54
Females		49	12.24	22.44	65.3	27.2	62.8
Total		170	18.32	15.88	65.29	48.55	51.45
41 to 60							
51 to death							



with the males. He also claims that granular kidney in relation to age incidence certainly increases with each decade parallel to that of atheroma.

The atherosomatous change in the arteries of Filipinos was determined by examination of 1,000 bodies in which the arterial changes were definitely recorded. The results obtained are not as conclusive as they might be, but they give a fair estimate of atherosomatous changes in Filipinos. Atherosomatous and associated cardiac and renal changes are without doubt important factors in the cause of death, at least after 40 years of age.

In tabulating this series of autopsies for atherosomatous changes, I have included sex, ages in decades, hypertrophied and normal hearts, and chronic interstitial nephritis and normal kidneys, noting whether or not they were associated with atheroma. Atheroma was divided into slight and marked changes; it was called slight when there were a few patches here and there throughout the aorta or in the coronaries, while those cases were called marked which showed numerous large patches, calcification, or ulcerative changes. A kidney was called chronic interstitial nephritis if it showed fibrosis, multiple small cysts, chronic diffuse nephritic changes, or arteriosclerotic changes. The heart was called hypertrophied from increase in size and weight, and it was not specified as to whether or not it was the entire heart.

The results obtained from an examination of the arteries, hearts, and kidneys of 1,000 Filipinos are summarized in Table IV.

#### DISCUSSION OF ATHEROMA

The successive decades between 0 and 40 years show a more or less constant and proportional increase of atheroma with associated hypertrophy of the heart and chronic interstitial nephritis. However, the decades between 41 years of age and death show a sudden great increase of atheroma with associated hypertrophy of the heart and chronic interstitial nephritis. This great increase of all three associated conditions is the most significant and important fact brought out by the tables and at least is indicative that they are probably a large factor in the cause of death after 41 years of age. The tabulation of the changes as they occurred in each sex does not show any great difference between the sexes. Of those examined for atheroma who lived beyond the age of 40 years, 23.84 per cent were females. However, a greater percentage of the females over 40 years of age showed atherosomatous changes than did the males, while under the age of 40 years a smaller percentage of females showed

atheromatous changes than did the males. The heart changes recorded show that after the age of 40 hypertrophy of the heart as associated with atheroma is found to occur in the males almost twice as frequently as in the females. The kidney changes recorded show that after the age of 40 years chronic interstitial nephritis is found almost as frequently in the females as in the males and is found in both on an average of 75.77 per cent.

#### ETIOLOGIC AGENTS OF ATHEROMA

Among the conditions which enter for consideration as possible factors in producing atheroma with its associated heart and kidney changes in Filipinos are increased blood pressure, syphilis, strains, alcohol, and chronic intestinal disorders.

*Blood pressure.*—Recently the blood-pressure picture in Filipinos was determined by Concepcion and Bulatao.(2) Their experiments show that the average blood pressures in Filipinos expressed in millimeters of mercury are as follows: Between the ages of 15 and 40 years the systolic pressure is 114.45, the diastolic pressure 80.76, and the pulse pressure 33.69; above the age of 40 years the systolic pressure is 131.27, the diastolic pressure 88.72, and the pulse pressure 42.55. The systolic pressure of the Filipinos is very much lower than that of Americans living in temperate climates (Woley), but is the same as that of Americans living in the tropics whose ages range between 18 and 50 years, the average being 26.6 years.(1) These findings suggest that in the tropics systolic pressures are very much lower than in temperate climates and that with increase of age there is a general rise of systolic, diastolic, and pulse pressures in the Filipinos.(2)

An examination of the preceding statements, which give a fair estimate of the blood-pressure picture in Filipinos, is at least indicative that blood pressure is not a primary factor in producing atheroma in Filipinos.

*Syphilis.*—Syphilis appears to be on the increase in the Philippines, but will only be mentioned from a statistical view. The amount of syphilis cannot be stated in percentage for the entire Islands, but the Wassermann laboratories show it to be very common. A conservative estimate regarding the number of patients treated in the Philippine General Hospital suffering from syphilis was 3 per cent. Although the Philippine Health Service reported that 1.4 per cent of 16,431 cases were treated in the wards of the Philippine General Hospital during 1914 for syphilis, this did not include the incidence in 25,000 or more dispensary cases, which would undoubtedly make a much higher

percentage. Also it does not include other conditions which in some instances are no doubt of syphilitic origin, such as still-births. A review of 712 autopsies at Manila, (8) performed during 1913, showed 21 cases presenting recognizable syphilitic lesions. However, there were only 11 of these occurring in Filipinos, but of these 11 there were 9 cases where the aorta was involved. This substantiates a fact mentioned by Crowell that where syphilis is recognized at autopsy in Filipinos the vascular lesions are the most frequent. In my series of 1,000 atheroma cases 4.83 per cent were definitely recognized as syphilitic in origin. There is the probability that a number of syphilitic atheroma cases were masked by an extensive atheroma other than syphilitic and were thus overlooked at autopsy.

*Chronic intestinal disorders.*—A personal examination of the entire intestinal contents of more than 1,000 autopsies shows that the intestines of from 80 to 90 per cent of subjects are laden with faecal material containing one, two, or more types of intestinal zoöparasites. It seems evident that such a condition extending throughout years must produce a chronic toxæmia of intestinal origin. Clinical observation shows that constipation is the rule rather than the exception among the class of patients entering the hospitals. From the amount of data at hand on this subject any conclusion is hypothetical, but basing such a conclusion on the preceding statements, it appears that chronic intestinal disorders leading to chronic toxæmia are probably an important factor in the production of atheroma in Filipinos.

*Strains.*—Strains resulting from heavy and continued manual labor are found among such classes as farmers and stevedores, and a small percentage is found among workers in mines and railroads. However, the Philippines does not possess the industries which require large numbers of laborers who perform heavy manual labor over a long period of time. The women of the working classes usually perform heavy work, such as carrying burdens on their heads. On the whole, it is doubtful whether any importance can be placed on strains as a prime factor in producing atheroma or other arterial changes among the people of this country.

*Alcohol.*—Alcoholic drinks are partaken of by the Filipinos throughout the Islands, but not as a rule to the extent of intoxication. It is rare that a Filipino is seen under the influence of alcohol. There are a number of locally made drinks, such as tuba, tapuy, vino, basi, and ginebra, some of which contain large

amounts of alcohol. Statistics compiled by the Bureau of Internal Revenue show that there is an annual domestic consumption of between nine and ten million proof liters of locally distilled spirits. This does not include the spirits from illicit stills. The statistics for 1915 showed that there were found in the Islands 108 illicit stills, while there were 75 registered stills. The above statistics do not include imported spirits.

#### ANEURISMS

The aneurism incidence as seen at autopsy in Filipinos has been tabulated primarily for comparison with Rogers's determination of aneurism incidence in the natives of India. A knowledge of the incidence of aneurisms in tropical people may also be of value for comparison with their incidence in people of temperate climates. Such a comparison may throw light upon the alleged greater virulence of oriental syphilis, in so far as this may be manifested by the production of aneurisms. Practically all of the aneurisms of this series have been found in cases of sudden death, and all showed evidences of syphilis other than the aneurism itself.

Rogers reports that the post-mortem records of the Calcutta Medical College showed 30 aneurisms among 5,900 autopsies, making an incidence of 0.5 per cent, although among the natives alone the aneurism incidence was 0.86 per cent. He claims that syphilis is appallingly common among the class of natives who enter the hospitals.

TABLE V.—*Race incidence of aneurisms in India.* (5)

Race.	Aneurisms.	Proportion.	Subjects.	Race incidence.
Europeans.....	9	81.1	7.0	2.2
Hindus .....	11	37.0	27.4	0.28
Mohammedans .....	8	27.6	21.8	0.62
Native Christians .....	1	3.4	3.8	0.45
Total .....	20	68.9	98.0	0.86

In determining the incidence of aneurisms in Filipinos, I have included all aneurisms found in 5,400 autopsies. The race, sex, and age incidence are summarized in Table VI, while Table VII shows the more important features of an analysis of all the aneurisms with the associated lesions of rupture, atheroma, chronic interstitial nephritis, and hypertrophy of the heart.

TABLE VI.—Race, sex, and age incidence of aneurisms in the Philippines as seen at autopsy.

Race.	Autopsies examined.	Aneurisms.	Average age of occurrence.	Sex incidence.	
				Years.	Per cent.
Filipinos .....	4,969	19	48.42	0.382	89.5 11.5
Chinese .....	228	10	42.12	4.34	100.0 0.0
Japanese .....	54	1	26.0	1.85	0.0 100.0
Americans .....	114	9	39.2	7.88	100.0 0.0
Europeans .....	35	1	42.0	2.08	100.0 0.0
Total .....	5,400	40	.....	.....	.....

Table VI, it will be seen, shows the aneurism incidence in Filipinos to be 0.382 per cent, which is very low when compared with the aneurism incidence in Chinese, 4.34 per cent, and the aneurism incidence in Americans, 7.88 per cent. This low aneurism incidence in Filipinos is similar to the low aneurism incidence in the natives of India, which Rogers gives as 0.36 per cent.

#### ETIOLOGIC AGENTS AND LESIONS ASSOCIATED WITH ANEURISMS

*Syphilis.*—Syphilis is probably the cause of all the aneurisms of this series, and in all cases there were other associated lesions of syphilis, such as arteritis, gummatous, and osteitis. The prevalence of syphilis in the Philippines is discussed under atheroma.

*Blood pressure and strains.*—In this series of aneurisms there could not be obtained any reliable histories or recorded blood pressures. Some of the cases in Filipinos occurred in farmers and sailors, while in the Chinese some occurred in those who performed heavy manual labor; in the Americans and Europeans the cases varied from those who performed heavy manual labor to those who did clerical work. The case occurring in a Japanese was in a prostitute.

*Hypertrophy of the heart.*—Hypertrophy of the heart occurred in 67.5 per cent of all cases, while 32.5 per cent were either normal in size or smaller than normal.

*Chronic interstitial nephritis.*—Chronic interstitial nephritis occurred in 65 per cent of all the cases, while 35 per cent showed apparently normal kidneys.

TABLE VII.—Classification of aneurisms and associated lesions as seen at autopsy.

Artery affected.	Aneurisms.	Per cent.	Atheroma.	Hypertrophy of heart.	Chronic interstitial nephritis.	Site of rupture.													
						Slight.	Mark-ed.	Pres-ent.	Ab-sent.	Peri-cardial sac.	Right.	Left.	Pleural sacs.	Ab-dom-en.	Bron-chi.	Eso-phag-us.	Medias-tinum.	Trachea.	Not ruptured.
Ascending arch of aorta	17	42.5	3	14	12	5	9	8	9	0	0	0	0	0	0	0	0	0	8
Transverse arch of aorta	8	20.0	0	8	4	4	5	5	3	1	0	2	0	1	0	1	2	1	1
Descending thoracic aorta	11	27.5	0	11	8	3	8	3	0	0	0	4	0	1	2	0	0	4	4
Abdominal aorta	1	2.5	1	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0	0
Subclavian artery	1	2.5	0	1	0	1	0	1	0	1	0	1	0	0	0	0	0	0	0
Femoral artery	1	2.5	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Cerebral artery	1	2.5	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1
Total	40	100.0	4	36	27	13	25	15	10	1	6	1	2	1	2	1	2	1	15

*Atheroma.*—Atheroma occurred as marked atheroma in 90.0 per cent of all cases and as slight atheroma in 10.0 per cent. The type of atheroma in all cases was syphilitic, although in several cases there was associated the calcified type seen in old age. However, from a preceding statement under atheroma that 4.33 per cent of all our atheroma cases were syphilitic, and since the majority of gross syphilitic changes in Filipinos are seen in the arteries, while the aneurism incidence is only 0.382 per cent, there is evidently a large excess of syphilitic arteritis to form a base for aneurism formation. It would be safe to conclude that syphilis of the vessels does play an important part in the production of aneurisms in Filipinos.

#### DISCUSSION

Here in the Philippines an examination of the autopsy records shows a low aneurism incidence among Filipinos, 0.382 per cent, which is similar to the low aneurism incidence seen at autopsy among the natives of India (0.36 per cent). From this low incidence of aneurisms in the races, it seems that syphilis in the tropics has less predilection for the arteries of the natives than it has for the arteries of northern races residing in the tropics. Probably what is more nearly correct is that syphilis produces more pathologic effects on the arteries of northern races in the tropics than it does upon the native born.

The high aneurism incidence as found among the Americans is considerably in error, because the majority of the American dead examined at the city morgue are examined on account of unexplained sudden death, while the larger number of dead Americans are not autopsied. Nevertheless, in consideration of the fact that there are only about 0.15 per cent as many Americans residing in the Islands as Filipinos, it appears that the aneurism incidence in Americans in Manila is considerably greater than in Filipinos.

There were five cases in which there occurred multiple aneurisms. In one case two aneurisms were found, one affecting the femoral artery and the other the ascending aorta, which is reported more completely as follows:

#### A CASE OF ANEURISM OF THE FEMORAL ARTERY AND OF THE AORTA

A survey of the aneurisms found in the 42,000 clinical records from the Philippine General Hospital and the 5,400 autopsy records from the College of Medicine and Surgery, of the University of the Philippines, shows that this case is the only femoral aneurism recorded. However, primarily the case is reported on account of the large size of the femoral aneurism.

*History.*—The patient is a Chinese male whose age is 41 years. He entered Bilibid Prison on January 18, 1916, for a term of four months' detention and was admitted to the prison hospital complaining of a continual chest pain which had been present for the past two months. The pain was first noticed after performing heavy manual labor, and it has become so severe that the patient breathes with difficulty. (No further description of the pain is recorded.) Upon further physical examination a large pulsating tumor was found in the right inguinal region below Poupart's ligament. The patient had not complained of this pulsating tumor, but had applied some form of dressing, which produced necrosis of the tissues over the apex, and this was accompanied by continual oozing of blood. The entire right lower extremity is edematous, and the skin is tightly stretched. No definite history could be obtained concerning the length of time that the tumor mass was present nor concerning syphilitic infection.

*Laboratory report.*—A Wassermann test performed by the Bureau of Science, January 24, 1916 (87931-C), was negative.

The urine was normal.

A tentative diagnosis was made of malignant tumor or aneurism. The surgeon in charge advised an operation to prevent the loss of blood from the tumor mass.

*Operation.*—Spinal anesthesia was employed by using 80 milligrams of stovaine. The stovaine was administered at 3.35 in the afternoon, January 24, 1916, and the operation began at 4.15 and was completed at 4.41.

An incision was made over Poupart's ligament, and the iliac artery was ligated extraperitoneally above the tumor mass. A section of tissue from the apex was removed for histological examination; it showed evidences of an arterial wall. The entire right lower extremity was then placed in hot packs. The patient appeared to be in very good condition when seen at 8.30 in the evening, but suddenly died at 9.15, January 24, 1916, about four and one-half hours after the operation.

The autopsy findings are as follows. Anatomical diagnosis: Chronic aortitis with aneurismal dilatation of the aorta (syphilitic); chronic parenchymatous degeneration of the heart (syphilitic); aneurism of the femoral artery (syphilitic); chronic diffuse nephritis; pneumoconiosis; chronic miliary tuberculosis of the lungs; chronic adhesive fibrous pleuritis; and some edema and congestion of meninges.

The body is that of a rather large, poorly nourished, adult Chinese male, aged 41. The skin is yellowish brown. The hair is black, straight, coarse, rather long, and limited to the pubes, axillæ, and scalp. The eyes are apparently normal. The teeth are carious, and the mucosa of the mouth is pale and somewhat necrotic over the gums. Rigor mortis is present throughout the body, and suggillation is present on the dependent portions of the body. Lying in the right femoral region involving an area over Scarpa's triangle there is a firm, bulging, hemispherically shaped mass which measures from 10 to 12 centimeters in diameter; its apex is 5 to 6 centimeters above the surrounding skin surface. The skin covering the mass is tightly stretched, but apparently normal, except at the apex, where it has a greenish necrotic appearance, and upon pressure some thin blood-tinged fluid oozes from it. After dissecting the skin from the entire mass and opening it, it is found to be filled with newly formed blood clot, which has the consistence of chicken fat. The walls of the mass are formed by a dilatation of the femoral artery producing an elongated, irregular, ovoid-

shaped aneurism which measures 11 to 12 centimeters in the long diameter and 7 to 8 centimeters in the short diameter. The walls are firm and retain their shape. They measure 3 to 4 millimeters in thickness. The intimal surface of the aneurism is roughened in numerous places with flat, soft yellowish plaques which average 0.5 to 1 centimeter in diameter and about 2 millimeters in thickness.

The upper extremity of the aneurism lies immediately below Poupart's ligament, while the lower extremity lies at the opening of Hunter's canal. Both the iliac artery leading into the aneurism and the continuation of the femoral artery from the aneurism are apparently normal.

An operative wound had been made over Poupart's ligament, and the iliac artery had been ligated just above the aneurism.

On section of the body there is found a very small amount of subcutaneous fatty tissue. The muscle is a pale reddish brown and is somewhat soft in consistence.

*Abdomen*.—The serosa of the small intestine has a light grayish color, that of the large intestine is rather pale, and the entire serosa is moist. The abdominal cavity itself is moist, but does not contain any free fluid. The diaphragm is located at the fifth rib on the right and the sixth on the left side. The abdominal viscera lie in normal relationship to each other.

*Thorax*.—The thymus is atrophied.

*Pleural sacs*.—Both pleural sacs are obliterated with fibrous adhesions over the apex and somewhat posteriorly, while anteriorly they are free from adhesions. The parietal pleura has a grayish color, while the visceral pleura shows a blackish color over most of its surface.

*Lungs*.—The lungs themselves are very large. The entire upper lobes of both lungs are consolidated and hard in consistence. On section the upper lobes cut with very much resistance, showing a surface which is smooth, very compact, and black, but in some places there are elevated whitish areas of 1 to 2 millimeters in diameter, the entire cut surface having the appearance as though cutting through a lump of coal. The lower lobes of both lungs are voluminous and float high in water, although the upper portion of the lower lobe of the right lung shows a condition similar to the upper lobes of both lungs. Section through the lower lobes shows a rather smooth surface of normal compactness which is greenish black and moist. The bronchi have a reddish color and contain mucoid material.

*Heart*.—The parietal pericardium is pale, smooth, and thin. The pericardial sac is about normal in size and shape and is free from adhesions; it contains a normal amount of fluid. The epicardium is rather pale and covers some fat; in the other places it is smooth and thin. The heart itself is somewhat enlarged, the tricuspid valve admitting almost four fingers, the mitral valve barely three. The left auricle is considerably distended with blood, and the right auricle is also distended with blood, while the right ventricle and left ventricle both appear to be enlarged, and the walls are slightly thicker than normal. The muscle is pale brown and is very soft and rather flabby; the cut surface is smooth and dull. The endocardium covering the aortic and mitral valves is somewhat thickened, while throughout the remaining portion of the heart it is pale, smooth, and thin. The blood is coagulated, forming coagulum of chicken-fat consistence.

*Aorta*.—The aorta extending from the aortic valve up to and involving the transverse arch is considerably dilated and at one place shows an outpouching over a circular area of 6 to 7 centimeters. This outpouching is as

much as 2 centimeters deep in places and begins just above the aortic valve. The walls of the entire portion are inelastic, and the intima is roughened with plaques which are flat, soft, elevated, and whitish to yellowish. These plaques measure from 0.5 to 1 centimeter in diameter and about 2 millimeters in height. Throughout the remaining portion of the thoracic and abdominal aorta the intima shows the presence of some whitish to yellowish elevated plaques of 0.5 to 1 centimeter in diameter. The iliac arteries are apparently normal.

*Spleen.*—The spleen is about normal in size and rather soft and is bluish gray. The capsule is smooth. The spleen cuts with some resistance, showing a smooth reddish surface upon which the interstitial tissue is prominent. From the cut surface exudes some blood-tinged fluid.

*Adrenals.*—The adrenals show no appreciable change from normal.

*Kidneys.*—The kidneys are about one and a half times the normal in size, but they are about normal in shape. They are surrounded by a small pad of fat, and they are firm. They cut with resistance, showing a smooth surface upon which the pyramids are regular in outline and pale, with a pinkish tint and with some red linear markings at the bases; while the cortex varies in thickness, from thinner to thicker than normal, and the entire cortex is pale, with a pinkish tinge, and appears to be minutely granular. The capsule strips with considerable resistance, showing a surface which is smooth in places and somewhat roughened in others and which is pale. The pelves are apparently normal.

*Intestines.*—The intestines are apparently normal.

*Liver.*—The liver is brownish. The capsule is smooth. It is about normal in shape and size. It cuts easily; upon the cut surface the lobules are plainly visible, although they appear to be slightly paler than normal, and the outlines are pale. The bile ducts and vessels show no appreciable change. The gall bladder contains some thick, viscid greenish bile, and its mucosa and walls are apparently normal.

*Urinary bladder.*—The urinary bladder is contracted and empty. Its mucosa is pale and smooth throughout.

*Brain.*—The dura mater strips easily and is pale and smooth. Beneath the pia-arachnoid there is an excess of watery fluid, but the vessels show no appreciable change from normal.

#### HISTOLOGY

Sections were made from the femoral aneurism and from the aneurismal dilatation of the aorta. The sections included a raised plaque upon the intima and were stained with haematoxylin and eosin and were also stained for spirochetes by the Levaditi method.

*Aneurism walls.*—There is a thickening of the intima which is composed of a noncellular hyalinlike substance which has its continuity broken in places. The media in places is infiltrated with round cells, which produce a slight spreading of the muscle fibers. The blood vessels of the tunica externa have thickened walls and narrowed lumens and are surrounded with dense, round-cell infiltration and some endothelial leukocytes.

*Aortic walls.*—The aortic walls resemble the aneurism walls with the exception that there is more extensive cellular infiltration of the media with degeneration and a new-forming compact tissue. The vasa vasorum are also more extensively involved than are those of the femoral vessel.

The sections stained by the Levaditi method do not reveal any structures

which can be absolutely identified as *Treponema pallidum*, but there are structures which resemble them.

*Heart muscle.*—Sections of the heart muscle stained by the Levaditi method do not reveal any evidence of *Treponema pallidum*.

#### CONCLUSIONS

1. The average duration of the life of Filipinos is shown by the statistics of the Philippine Health Service to be considerably below 40 years.

2. The cause of death before 40 years of age in the greater percentage of Filipinos is due to the tropical diseases.

3. The incidence of atheroma with associated hypertrophy of the heart and chronic interstitial nephritis increases suddenly after 40 years of age; this is an important factor in the cause of death after 40 years of age.

4. Chronic intestinal disorder leading to chronic toxæmia is probably the most important factor in producing such a high percentage of atheroma.

5. The aneurism incidence of Filipinos as seen at autopsy is 0.382 per cent.

6. The chief manifestation of syphilis in Filipinos, as seen at autopsy, is in the arteries in 80 to 90 per cent of the cases.

7. High blood pressures and strains do not appear to be important factors in the production of atheroma in Filipinos and probably not in the production of aneurisms.

8. These findings concerning vascular lesions seen at autopsy in the Philippines agree closely with the findings of Rogers in India.

#### REFERENCES

1. CHAMBERLAIN, W. P. A study of the systolic blood pressure and the pulse rate of healthy adult males in the Philippines, *Phil. Journ. Sci., Sec. B* (1911), 6, 467.
2. CONCEPCION, I., and BULATAO, E. Blood pressure picture of the Filipinos, *ibid.* (1916), 11, 135, 151.
3. HAMMACK, R. W. Syphilis in 712 autopsies. Reported before the Manila Medical Society (1914).
4. MENDOZA-GUAZON, MARIA PAZ. Study of the anatomicopathologic lesions in one thousand Filipino children under five years, *Phil. Journ. Sci., Sec. B* (1917), 12, 51.
5. ROGERS, L. Gleaning from the Calcutta post-mortem records, *Ind. Med. Gaz.* (1910), 45, 84-90, 124-127.
6. WOLEY, H. P. The normal variation of the systolic blood pressure, *Journ. Am. Med. Assoc.* (1910), 55, 121.

## SUBSTITUTION OF HUMAN BLOOD CELLS BY MONKEY'S RED CORPUSCLES IN PERFORMING THE COMPLEMENT FIXATION TEST FOR SYPHILIS<sup>1</sup>

By OTTO SCHÖBL and CARLOS MONSERRAT

(From the Serum Section of the Biological Laboratory, Bureau of Science,  
Manila)

The absence of natural hæmolytic amboceptor in human serum makes the use of antihuman amboceptor and human red cells preferable to those methods which employ antisheep hæmolytic system. However, there is a practical difficulty connected with this method, namely, the comparatively low titer of the anti-human amboceptor as usually obtained by immunization of rabbits with human red corpuscles. A considerable number of injections is necessary, and strictly fresh blood not always being available to a laboratory worker who happens to be without direct connection with a hospital or a similar institution, a high percentage of rabbits die before they yield serum strong enough to be useful for a test.

It occurred to us that, on account of the biologic relationship, monkey's red cells may probably behave in a similar way as human corpuscles in this respect. These animals, common in tropical countries, are inexpensive and easily maintained about the laboratory. Thus a supply of fresh blood is always at hand, since repeated bleedings taken directly from the animal's heart are tolerated without any apparent harm to the animals.

In order to establish the usefulness of monkey's red cells in performing the complement-fixation test for syphilis, the following question had to be answered:

1. It had to be determined whether or not human serum contains natural hæmolytic amboceptor toward monkey's red corpuscles.

2. The practicability of producing high value antimonkey hæmolytic amboceptor had to be established.

3. A series of comparative tests with sera submitted for routine examination had to be carried out to determine if there is any lessening in the accuracy of the test when monkey's red corpuscles are used as compared with the method in which human red cells are employed.

<sup>1</sup> Received for publication June, 1917.

With these points in view the following experiments were undertaken, the arrangement of which is evident from the tables.

TABLE I.—*Showing the results of searching for natural haemolytic amboceptor toward monkey's red cells in human sera.*

[c. h., complete haemolysis; m. h., moderate haemolysis; s. h., slight haemolysis; v. s. h., very slight haemolysis; n. h., no haemolysis.]

0.2 c. c. of inactivated patient's serum. Specimen No.—	Result after 0.5 c. c. of 4 per cent suspension of monkey red cells and complement 1:10.	0.2 c. c. of inactivated patient's serum. Specimen No.—	Result after 0.5 c. c. of 4 per cent suspension of sheep cells and complement 1:10.
11260.....	n. h.	c. h.	C O .....
11079.....	n. h.	m. h.	M M .....
11553.....	n. h.	v. s. h.	V B .....
14827.....	n. h.	v. s. h.	V N .....
9276.....	n. h.	c. h.	V R .....
5998.....	n. h.	c. h.	C G .....
32876.....	n. h.	n. h.	P .....
41258.....	n. h.	n. h.	A V .....
89477.....	n. h.	n. h.	R M .....
11582.....	n. h.	m. h.	F H .....
A A .....	n. h.	n. h.	G Y .....
T V .....	n. h.	s. h.	V G .....
P L.....	n. h.	c. h.	49590.....
H L.....	n. h.	n. h.	42008.....
M O.....	n. h.	c. h.	42276.....
N A.....	n. h.	c. h.	42289.....
G M.....	n. h.	c. h.	P G .....
Y B.....	n. h.	n. h.	M K .....
F C.....	n. h.	v. s. h.	M E .....
F A.....	n. h.	n. h.	M W .....

It is evident from the results of the tests of 40 sera collected at random over a period of several months that none of them, in the quantity used, contained a sufficient amount of natural amboceptor to cause haemolysis when brought in contact with red corpuscles of monkey and guinea pig's complement. However, the majority of the same sera contained a considerable amount of antisheep natural haemolytic amboceptor.

#### ANTIMONKEY HAEMOLYTIC AMBOCEPTOR

The difficulty in production of high-value antihuman haemolytic amboceptor has been already mentioned in this paper. In our experience the average number of injections necessary to produce useful serum amounted to at least five injections and the resulting

serum averaged 100 units per cubic centimeter, rarely 150, and never more than 200 units per cubic centimeter. Simultaneous intravenous and intraperitoneal injections gave the best results. Allowing an interval of four days between injections, from 10 to 15 cubic centimeters of serum were obtained in twenty-six days. That is to say, one rabbit yielded from 1,000 to 1,500 units. However, sera of not more than 50 units per cubic centimeter were frequently obtained. Considering the high mortality of the treated animals and the poor condition of the survivors, it will be appreciated that the production of antihuman haemolytic amboceptor requires a great many animals and involves a good deal of work, time, and expense.

Following are the records of animals immunized with monkey's red corpuscles.

Rabbit 1 received the usual number of injections of washed monkey's red cells, that is, five injections intravenously and five injections intraperitoneally at the same time. The period of immunization extended over fifteen days. Five days after the last injection the animal was bled. Two days later another bleeding was taken from the heart. Altogether 25 cubic centimeters of serum were obtained by both bleedings. The mixture of the two sera tested 4,000 units per cubic centimeter. The total amount of monkey's blood used for immunization was 7.30 cubic centimeters. This rabbit, three weeks after the immunization began, yielded 100,000 units and survived, thus being available for other purposes.

Rabbit 2 received three injections within eight days. The total amount of blood injected was 4.50 cubic centimeters. Five days after the last injection the serum of this animal tested 2,000 units per cubic centimeter.

Rabbit 3 received only two injections of monkey's red cells. The total amount of blood was 2.50 cubic centimeters. Its serum tested 100 units per cubic centimeter.

Rabbit 4 received but one injection of monkey's red cells. When tested five days after the injection, the serum had a titer of less than 20 units per cubic centimeter.

Following the usual scheme of immunization, in rabbit 1 a serum was obtained in three weeks, which was twenty times higher than the best average antihuman haemolytic serum; in rabbit 2 ten times higher serum was obtained in two weeks; and rabbit 3 yielded in nine days serum of the same titer as the average antihuman amboceptor obtained after five injections.

Rabbit 4, after one injection, gave serum of 20 units per cubic centimeter.

It follows from these experiments that two injections of monkey's red cells are sufficient to produce serum of 100 haemolytic units per cubic centimeter, which is useful serum for tests. This can be accomplished within thirteen days, using not more than from 2.5 cubic centimeters to 3 cubic centimeters of blood.

In Table II the results of comparative tests are given. In one series antihuman amboceptor and human red cells were used; in the other the same specimens of blood were subjected to a test in which antimonkey haemolytic system was employed. Otherwise the arrangement of the tests was identical in both series.

TABLE II.—*Showing comparative tests with antihuman and antimonkey haemolytic system.*

Specimen.	Antihuman haemolytic system.		Antimoneky haemolytic system.	
	Alcoholic antigen.	Cholester antigen.	Alcoholic antigen.	Cholester antigen.
M T	pos. ±	pos. +	pos. ±	pos. +
11967	neg.	pos. +	neg.	pos. +
10194	pos. 6 +	pos. 6 +	pos. 6 +	pos. 6 +
41770	neg.	pos. +	neg.	pos. +
C H	neg.	neg.	neg.	neg.
M	pos. ±	pos. ±	pos. ±	pos. ±
W	pos. 6 +	pos. 6 +	pos. 6 +	pos. 6 +
G	pos. ±	pos. ±	pos. ±	pos. ±
D	neg.	neg.	neg.	neg.
41824 C	pos. 8 +	pos. 8 +	pos. 8 +	pos. 8 +
FW	neg.	neg.	neg.	neg.
42195	pos. +	pos. 3 +	pos. +	pos. 3 +
42009	neg.	pos. 3 +	neg.	pos. 3 +
C C	neg.	pos. 3 +	neg.	pos. 3 +
M T	pos. +	pos. 6 +	pos. +	pos. 6 +
Or	neg.	neg.	neg.	neg.
42008	pos. ±	pos. +	pos. ±	pos. +
42276	pos. +	pos. 5 +	pos. +	pos. 5 +
42289	pos. 3 +	pos. 6 +	pos. 3 +	pos. 6 +
M G	neg.	pos. ±	neg.	pos. ±
M H	neg.	pos. ±	neg.	pos. ±
Mc C	neg.	neg.	neg.	neg.
Y K Y	neg.	neg.	neg.	neg.
12094	pos. 2 +	pos. 3 +	pos. 2 +	pos. 3 +
42312	pos. 3 +	pos. 6 +	pos. 3 +	pos. 6 +
M D	neg.	neg.	neg.	neg.
41841	pos. 5 +	pos. 6 +	pos. 5 +	pos. 6 +

Table II shows that the results of the complement fixation test with antimoneky amboceptor and monkey's red cells were identical with those obtained when antihuman haemolytic system was employed.

#### CONCLUSIONS

1. Human sera in quantities used for test were found to contain no antimonkey natural haemolytic amboceptor.
2. Haemolytic sera of higher value can be obtained by immunization of rabbits with monkey's cells than it is possible by immunization with human red corpuscles.
3. Comparative tests for diagnosis of syphilis carried out on samples collected at random gave identical results, whether antihuman or antimonkey haemolytic system was used.



## PROCEEDINGS OF THE MANILA MEDICAL SOCIETY

REGULAR MONTHLY MEETING, APRIL 2, 1917

The regular monthly meeting of the Manila Medical Society was held at 8.30 in the evening, April 2, 1917, in the College of Medicine and Surgery, with President Winter in the chair and with 12 members and 2 guests present.

Upon the suggestion of the president it was moved and seconded that the reading of the minutes of the last meeting be dispensed with, and the following applications for active membership in the society were recommended by the council for ratification by the society:

Lieut. Col. Joseph Taylor Clarke, M. C., Dr. Lane Bruce Kline.  
U. S. Army. Dr. José Eduque.  
Capt. Hew Bernard McMurdo, M. C., Dr. José S. Hilario.  
U. S. Army.

Colonel Manly moved that the society ratify the recommendation. The motion was seconded by Doctor Crowell, and the society voted favorably.

The society then voted to suspend its regular monthly meeting during May, June, and July and again to resume the meetings in August.

A vote of thanks was extended to the outgoing committee, who had so excellently arranged the program for the past three months. The program committee for August, September, and October was announced as appointed by the president:

Dr. C. H. Manlove. Dr. Daniel de la Paz. Capt. J. M. Willis.

Professor E. D. Merrill was not present to read his paper on Contact Poisons.

H. G. MAUL,  
Secretary-Treasurer,  
Manila Medical Society.

### SCIENTIFIC PROGRAM.

TREATMENT OF INTESTINAL AMOEBIASIS WITH SPECIAL REFERENCE TO IPECAC AND ITS DERIVATIVES<sup>1</sup>

By DR. B. C. CROWELL

Questions which have assumed importance in intestinal amoebiasis, aside from the pathogenicity of species, are the problem of

<sup>1</sup> This paper has been published in the *Journ. Am. Med. Assoc.* (1917), 69, 6.

carriers, the importance of species pathogenicity in treatment, and the periodicity of appearance of entamoebas. These are discussed. The experimental treatment of amoebic dysentery with ipecac and its derivatives is reviewed, and particular attention is given to Dobell's successful results with the emetine-bismuth-iodide preparation of Du Mez in amoebic dysentery cases and in ameba cyst carriers.

**DOES THE IRRITANT ACTION OF EMETINE HYDROCHLORIDE EXTEND TO THE KIDNEY?**

By Drs. DANIEL DE LA PAZ AND R. MONTENEGRO

The work was carried out in order to ascertain the irritant effect of hypodermic injection of emetine hydrochloride on the kidney. One milligram per kilogram of dog's weight was injected daily. Six dogs were used as controls: two received hypodermic injection of uranium nitrate, and four received a daily injection of sterile saline solution. The emetinized dogs died with typical symptoms of emetine poisoning. Emetine caused, in two dogs out of four, ecchymoses at the sites of injection, but in no case did its irritant action extend to the kidneys, although the drug eventually killed the animals.

R. B. GIBSON,  
*Editor of the Proceedings,*  
*Manila Medical Society.*

## PROCEEDINGS OF THE MANILA MEDICAL SOCIETY

REGULAR MONTHLY MEETING, AUGUST 6, 1917

The regular monthly meeting of the society was held at 8.30 in the evening, August 6, 1917, at the College of Medicine and Surgery, with President Ruth presiding. There were 33 members present and 8 visitors. The business brought before the society follows.

The minutes of the last meeting were read and approved as read.

The application of Major C. C. Billingslea, M. C., U. S. Army, for active membership was recommended by the council to the society for ratification. The secretary was instructed to place the name of Major Billingslea on the list of active members and then to transfer it to the nonresident list. It was also approved that Major Billingslea be informed by letter of the action taken and that upon his return to Manila he will be again taken up as an active member.

Doctor Crowell moved that the society accept the resignation of Colonel Francis A. Winter and that a letter be drafted and sent to him expressing the regret of the members in his departure and appreciation of his efforts as president of the society. The motion was seconded, and the society voted favorably.

H. G. MAUL,  
*Secretary-Treasurer,*  
*Manila Medical Society.*

### SCIENTIFIC PROGRAM

#### FURTHER OBSERVATIONS ON THE TREATMENT OF YAWS WITH CASTELLANI'S FORMULA

By DRs. LUIS GUERRERO, E. DOMINGO, and M. ARGÜELLES<sup>1</sup>

The high price and shortage of salvarsan and neosalvarsan (undoubted specific remedies for yaws) and objection on the part of patients to injection have made desirable the use of Castellani's formula for this disease. This formula consists of tartar emetic 0.065 gram, sodium salicylate 0.650 gram, potassium iodide 4.000 grams, sodium bicarbonate 1.000 gram, and water to make 30

<sup>1</sup> Presented by Doctor Domingo.

cubic centimeters. Children are given proportionate doses. On the first day one third of the dose is given three times in 120 cubic centimeters of water; on the second day, one dose twice; and on succeeding days, one dose three times daily. Administration of the formula is continued over from ten to fifteen days, and after an interval of from five to ten days is repeated for from five to fifteen days more. Of the 43 Filipino cases in which the treatment was continued, 24 completely recovered, 7 showed improvement of symptoms, 5 had relapses in two to five months after the lesions had entirely healed, and 7 showed no improvement. The results confirm Castellani's observation that the diverse manifestations of yaws heal under the influence of this formula. The treatment is particularly effective in recent infections. We believe that the continuation of the treatment after the lesions have healed (from five to ten days' treatment with intervals of from ten to fifteen days) will insure a permanent cure.

#### BONE AND JOINT LESIONS OF YAWS WITH X-RAY FINDINGS IN TWENTY CASES

By CAPT. HERMAN G. MAUL

Painful bone and joint involvements occurring in some cases of yaws were seen in the barrios of Las Piñas and Parañaque, Philippine Islands. Through the courtesies of Drs. Luis Guerrero, E. Domingo, and M. Argüelles, arrangements were perfected by which a group of one hundred cases of yaws was collected for study. The diagnoses of these cases were made by the histories, by clinical symptoms and manifestations, and by the demonstration of *Treponema pertenue* under the dark-field microscope in the cases where an open lesion was present and by a careful history of those without open lesions, so as to remove any doubt as to the diagnosis. Twenty per cent of the cases of this group of patients, as they presented themselves for treatment, suffered from bone and joint lesions. These patients were persuaded to come to the Department Hospital, Manila, for X-ray pictures and treatment. A röntgenological survey of all the bones of the body was made of each case, regardless of whether or not the patient complained of pain in the part X-rayed. Subsequent X-ray pictures were made in order to follow the progress of the lesions under treatment. In the majority of cases the lesions show as rarefied areas, irregularly oval or elliptical in shape, with the long axis parallel to that of the bone in which the lesions are located. The size varies from

the smallest discernible area to one which is 2 or 3 centimeters in length. The rarefaction presents moderately well-defined borders separating it from the unaffected bone and varies in translucency from the slightest differentiation of unnatural transparency to one simulating a perforation. Most of the lesions appear to originate in the interior of the bone, while a number can be seen as small excavations on its outer surface. When the lesion is on the surface of the bone, the periosteum is usually destroyed, but occasionally the cortex shows thickening and the periosteum is separated from the bone. In two cases of this series there is a general thinning of the cortex of the bone and a loss of the cancellous-tissue appearance. About 2 per cent of the cases show a nodular type of lesion, evidenced by swelling over the surface of the bone, with a localized thickening of the cortex, which sooner or later in the course of the disease shows rarefaction in its center. In the chronic lesions marked irregularity of the bony outline is evident, and the picture characteristic of the earlier lesions is more or less lost. The bone, as a whole, becomes deformed, and the growth of the bone is interfered with both in length and breadth. This dwarflike picture is most frequently noticed in the cases showing the lesions in the epiphyses. Within the joints the destruction is most frequently seen on the parts of the articular surfaces most exposed to trauma as oval or irregularly shaped excavations, making the outline of the articular surface rough and uneven. It is concluded from this series of cases that the joint pains complained of are due, in most part, to the presence of the lesions on the articular surfaces. With the exception of the 2 per cent of cases showing as a swelling over the surface of the bone, the X-ray picture is different from the bone lesion of syphilis, in that the periosteal proliferation and the thickening of the cortex of the bone are absent. Also, in the 2 per cent of cases where thickening of the cortex is present, the thickening remains localized, does not tend to extend along the whole length of the bone, and sooner or later shows rarefaction in the center of the lesion. The bone lesion of yaws may simulate (1) tuberculous or septic central abscess, (2) gumma, (3) hydatid cyst, (4) benign cyst, (5) fibrous osteitis, (6) enchondroma, (7) endothelioma, (8) secondary carcinoma, (9) myeloma, and (10) sarcoma. The differential diagnosis can be made only by combining the radiographic appearances with all clinical data, including the history, physical signs, and evidence of disease or tumor in other parts of the body. The Castellani treatment causes a gradual disap-

pearance of the bone and joint lesions. Salvarsan is a specific in these cases, and rapid regeneration of bone follows its use. Regeneration of the bone is complete at the site of the lesion if the destruction has not been too great.

Dr. Ricardo Fernandez corroborated Doctor Maul's findings and exhibited an X-ray plate of a case with lesions of yaws in the vertebræ.

R. B. GIBSON,  
*Editor of the Proceedings,*  
*Manila Medical Society.*

THE PHILIPPINE  
JOURNAL OF SCIENCE  
B. TROPICAL MEDICINE

VOL. XII

NOVEMBER, 1917

No. 6

MOHAMMEDAN MEDICAL PRACTICE IN COTABATO PROVINCE<sup>1</sup>

By LIBORIO GOMEZ  
(Cotabato, Cotabato, P. I.)

ONE PLATE AND SEVEN TEXT FIGURES

Cotabato Province is the largest province in area in the Philippine Islands, measuring 28,593 square kilometers. The number of inhabitants is not accurately estimated; the official census of 1903 places the population at 125,875. The following is an estimate appearing in the annual report for 1915, of the Provincial Governor of Cotabato, regarding the non-Christian population of the province:<sup>2</sup>

TABLE I.—*Non-Christian population of Cotabato Province.*

Mohammedan:	
Maguindanao	
Maranao	
Iranun	
Sangil	
Samal	
Sulug (Joloanos)	
Pagan:	
Manobos and Bagobos	15,000
Bilanes	8,000
Tirurayes	5,000
Tagabilis	1,000

<sup>1</sup> This is the first of a series of reports on the local medical practices in the Department of Mindanao and Sulu, suggested by the Chief Health Officer, Dr. Jacobo Fajardo.

<sup>2</sup> See also Beyer, H. Otley, Population of the Philippine Islands in 1916. Philippine Education Co., Inc., Manila (1917), for the most recent estimates.

The Maguindanao people are the most numerous and most powerful people in Cotabato Province; they occupy the whole valley of Cotabato and are scattered along the coast, but usually never live up the hills. The Maranao live in the range of mountains between Lanao and Cotabato. The Sañgils live in Sarangani Island. The Iranun live along Mulitabug River and also along the coast. There are a few Samals living in Bongos Island and along the sea coast wherever their vintas happen to stop. A few hundred Joloanos have settled on one end of Bongos Island.

There are two kinds of Manobos: Manobos living on the Apo range (Kidapawan region), who are mixed with Bagobos, and there are Manobos living on the mountains along the sea coast south of Lebak. The Bilans live on the mountains of Matutum region and on the southern range of mountains between Davao and Cotabato. The Tirurayes live on the hills of the municipal district of Auang and on the hills along the sea coast between Cotabato and Lebak. There are a few Tagabilis living on the hills along the sea coast between Kran and Sarangani Bay.

The main occupation of the different tribes is agriculture and to some extent hunting and fishing. The Samals, however, live exclusively by fishing.

The commonest diseases are: Malaria, tuberculosis, and diseases of the skin, as an example tinea circinata (dhobie itch). In this report I shall treat mainly of the medical practice among the Maguindanaos, which is typical of the practice of the Mohammedan (Moro) population in Mindanao.

The following diseases and conditions are recognized by the Maguindanaos:

TABLE II.—*Diseases and conditions recognized by the Maguindanaos.*

<i>Abas</i>	Measles
<i>Anga</i>	Chicken pox
<i>Bacatau</i>	Yaws
<i>Bakil</i>	Yaws of palmar and plantar surfaces
<i>Barirang</i>	<i>Ascaris lumbricoides</i> infection
<i>Batuc</i>	Cough
<i>Beneg</i>	Gotide
<i>Bilas</i>	Conjunctivitis
<i>Bingki</i>	Mumps
<i>Buguis-casila</i>	Dhobie itch or tinea circinata
<i>Buguis-murus</i>	Tinea imbricata
<i>Bulay</i>	Otitis
<i>Bungcaut</i>	Keratoderma plantaris et palmaris
<i>Bunug</i>	Insanity
<i>Buransi</i>	Stomatitis or glossitis with white patches or membrane

TABLE II.—*Diseases and conditions recognized by the Maguindanaos*—Cont'd.

<i>Busucúl</i>	Indigestion
<i>Cabisú</i>	Deafness
<i>Cabutá</i>	Blindness
<i>Caludusan</i>	Abortion
<i>Calugú</i>	Wart
<i>Catal or ibul</i>	Furunculosis
<i>Catú</i>	Abscess, chronic
<i>Curbau</i>	Œdema of legs and abdomen. Beriberi
<i>Darati</i>	Tubercular adenitis and ulceration of neck
<i>Dudsul</i>	Sty
<i>Garak</i>	Neuralgia
<i>Ila</i>	Pigmented mole
<i>Ing</i>	Carbuncle
<i>Ipul</i>	Leprosy, tubercular
<i>Kaluli</i>	Scabies
<i>Kudep</i>	Colo-colo (retraction of penis)
<i>Lacap or siruñgan</i>	Day blindness
<i>Lamlam</i>	Eczema or itch of the scrotum and penis
<i>Langilau</i>	Headache
<i>Lebag</i>	Tumor or inflammation
<i>Lumasá</i>	Coryza
<i>Magudu</i>	Diarrhoea
<i>Magudu sa rugu</i>	Dysentery
<i>Manu-manucan</i>	Night blindness
<i>Mapansi</i>	Cachexia, anaemia
<i>Mauaga</i>	Abscess
<i>Mayau</i>	Fever
<i>Mayau-matingau</i>	Malaria
<i>Muta-mudu</i>	Cholera
<i>Pali</i>	Wound in general
<i>Pamagat</i>	Yaws, articular symptoms
<i>Pamari</i>	Keratoma plantaris sulcatum. Same as bakil, with fissuration
<i>Pambahuyen</i>	Epilepsy
<i>Pamunus</i>	Acne vulgaris
<i>Pamuti</i>	Leprosy
<i>Panau</i>	Tinea versicolor
<i>Panú</i>	Smallpox
<i>Pangater</i>	Muscular rheumatism of legs in old people
<i>Pasmá</i>	Fever, believed to be internal
<i>Pedsá</i>	Large furuncle, usually single
<i>Pigket or nasadir</i>	Paralysis
<i>Putic</i>	Leucoderma
<i>Rastun</i>	Ulceration of palate and nose (es-pundia)
<i>Ratiun</i>	A kind of poisoning believed to kill instantly

TABLE II.—*Diseases and conditions recognized by the Maguindanaos—Cont'd.*

<i>Rayur</i>	Pthysis
<i>Saguiap</i>	Erysipelas. Herpes zoster
<i>Sakit</i>	Pain or disease located anywhere
<i>Sakit a mama</i>	Disease of man, gonorrhœa
<i>Salabi</i>	Chilblains
<i>Salannat-iblis</i>	Pain or disease due to the devil
<i>Salilau</i>	Stomatitis, coated tongue
<i>Sedsed</i>	Circinate eruption of yaws or any serpiginous eruption or sore
<i>Taguitic</i>	Difficulty in urination
<i>Takendi</i>	Dysentery. This term is applied when there is an abundance of mucus mixed with blood
<i>Tebpig</i>	Lepra. Any chronic ugly ulcer
<i>Tumiti sa nana</i>	Gonorrhœa
<i>Uasir</i>	<i>Oxyuris vermicularis</i> infection
<i>Ugam</i>	Pharyngitis and laryngitis
<i>Ulag</i>	Deep pain in plantar surface of foot, supposed to be transmitted to leg. Rheumatism of foot
<i>Ulapig</i>	Cold feeling, but not actual ague, specially in old people, associated usually with pangater
<i>Uled</i>	Worms, intestinal
<i>Umau</i>	Dumbness
<i>Umes</i>	Asthma
<i>Urac a ating</i>	Prickly heat

## CAUSATION OF DISEASE

The Maguindanaos attribute diseases to a variety of causes, such as poison, hunger, wind, sun, unfulfilled customs, promises or oaths, and animalcules, but the most frequent causes, however, are malignant spirits.

During the recent cholera epidemic in Cotabato Province (1915) people quarantined themselves against all strangers, and several persons were detained, searched, and threatened bodily harm because they were suspected of carrying poison which caused the cholera. In the disease called *pasmá* (fever) the symptoms differ according to the causative factor: from "hunger," cold all over the body first and fever afterward; from the "wind," fever inside and cold outside of the body; from the "sun," fever outside and cold inside; from "getting wet," the same symptoms as from wind. *Pasmá* is more liable to follow if a person gets wet or takes a bath while the sun is at its zenith. They have no conception of microbes, but they believe some minute worms, *kanam*, to be the cause of scaly skin diseases and

also recognize small parasites, *cagau*, which they frequently see in the common itch (scabies).

The practice called *tauacal* is often done in order to find the cause of the disease in regard to customs, promises, and oaths, deducing at the same time the method of treatment. An egg is divided in five equal areas radiating from the smaller end, and on the areas thus outlined the following words are marked: *asal*, *sapa*, *panaman*, *samayá*, and *umur*, as shown below:

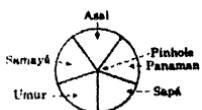


FIG. 1. The smaller end of the egg.

The egg is arranged in a coconut shell so as to stand up straight, a pinhole is made at the center of its smaller end, and after praying God to indicate the true nature of the disease, a piece of burning charcoal is applied at the bottom of the egg. The heat dilates the air space of the egg and expels some of its contents, and according to the area in which they are spilt, the cause of the disease is indicated. In the area of *asal* the patient is sick because he forgot to follow some of the customs of his ancestors, such as praying, giving alms, etc.; in *sapá* the patient did not fulfill an oath taken on the Koran; in *panaman* he failed to fulfill an unspoken promise; in *samayá* he failed to fulfill a spoken promise; in *umur* the cause of the disease may be anything, but the patient will irremissibly die.

Some panditas believe that there is a different cause for the diseases according to the day of the week such a disease began. A disease beginning on Sunday is caused by the devil; a disease beginning on Monday is caused by the wind; on Tuesday, by water; on Wednesday, by the sun; on Thursday, by hunger; on Friday, by an agent acting while one is asleep; and on Saturday, by an internal wound.

*Satan* and the rest of the devils and ghosts are credited with other diseases, the so-called *tinembas sa busau*, which are intense internal pains, such as colic, supposed to be internal wounds produced by the devil by striking a person with a leaf of cogon or with the midrib of a buri or coconut leaf, but which makes no marks on the outside.

Development of disease in one person through the spiritual agency or incantations of another, *papapantac* (analogous to the *mancuculam* of Luzon), is commonly believed. The people

of Lianāgan, a place on Illana Bay, in Lanao Province, are greatly feared because they are reputed to know this art. The papapantac prays for seven days, because the birthday of any person must have been one of the seven days of the week, and during these days he abstains from washing his anus and external genitalia after performing an act of nature. The papapantac makes a human form out of clay or tallow, or draws a human figure on paper, or uses an egg or a lemon, on which are marked both the earthly and heavenly names of the person whom it is desired to make sick and his place of residence. The human figure is placed in cold water, on the fire, exposed to the sun and rain, or pricked with needle or knife, according to the kind of disease on the part of the body where suffering is desired. A tail of buri is attached to the egg or lemon, and after the seven days of prayer, the egg or lemon is inclosed in a box and allowed to fly to the person to whom injury is desired.

To counteract the influence of the papapantac or to avoid other kinds of evil, the Moros place under the mattress of their beds a goat skin with various colors and offer a prayer, *tindig*, before going and before leaving the bed.

#### PROGNOSIS OF THE DISEASE

When a person is sick, the probable outcome is found by opening the Koran and determining the hour, day, month, and tide in which the disease began.

The opening of the Koran is done by the highest ranking pandita (priest) or hadji (person who has been in Mecca) around. Prayer is made, asking God that light be given on the disease in question, the Koran is opened with the eyes closed, and the first consonant letter of the seventh line of the page to the right is noted. This letter is called *aul*. Then seven sheets of the Koran are counted to the left, beginning with the sheet next to the page where the *aul* was noted, and the first consonant letter of the seventh line of the page to the right (left face of the seventh sheet) is also noted. This letter is called *agir*.

Every consonant letter in the alphabet has a meaning with regard to sickness and other conditions or enterprises. The following is the list of the letters with their significance in regard to sickness, according to Saika Datu-sa-Calangganan.<sup>2</sup>

<sup>2</sup> The Arabic characters and their names and equivalents are as furnished by the author of this paper.—THE EDITORS.

The following are good; sickness will be followed by rapid cure:

Letter.	Name.	Latin equivalent.
ا	Alip	Aspiration
ت	Tsa	Ts
ج	Jaa	J strong
د	Dal	D
ر	Ra	R
س	Sin	S
ط	Ta	T
ق	Kap	C or Q
م	Min	M
ن	Nun	N
ه	Ha	H
ء	Ambia	Expresses no letter
ي	Ya	Y

The following are bad; the disease will last long, but will not be followed by death:

Letter.	Name.	Latin equivalent.
ب	Ba	B
ج	Ja	J
د	Dsal	Ch
ز	Zay	Z
خ	Xim	X
س	Sada	S

Letter.	Name.	Latin equivalent.
ل	Lad	L
ل	La	L
أ	Ain	H (silent)
غ	Gain	G
ك	Kap	K
ل	Lam	L
ل	Lamalip	La
ع	Uau	U consonant

The following are very bad; sickness will be soon followed by death:

Letter.	Name.	Latin equivalent.
ت	Ta	T
ع	Geim	Gu
ف	Pa	P

Some other panditas and hadjis do not agree entirely with the significance of certain letters as above noted. Datu Mastura, of Nuling, gives the following significance of the letters:

Good.	Equally good and bad.	Bad.
Alip	Geim	Ja
Ba	Dsal	Zai
Ta	Ta	Sin
Tsa	La	Xim
Jaa	Gain	Ain
Dal	Mim	Kap (strong)
Ra	Ya	Lam
Sada	Uau	Lamalip
Lad	Pa	Ambia
Kap		
Nun		
Ha		

In weighing the probable outcome of the disease by the aual and the agir found in the Koran, the agir is much more important. If both letters or if the agir alone is of bad significance the prognosis of the disease is bad. If both letters or if the agir is good the prognosis is good. If the aual and the agir found are the same letter, a *tangung* results; the prognosis is bad, especially when they are both the letter alip; then the patient will irremissibly die.

The prognosis of the disease is influenced by the *cutica*, or the hour period (*wactū*), in which it begins. The good cutica in regard to disease are *maisuara*, *sry*, and *bisnu*, and the non-favorable cutica are *kala* and *barahama*. During the first day of any month the *maisuara* occupies the hour period *subu*, which is about from 6 in the forenoon to 2 in the afternoon; the *kala* reigns during the period of *lujur*, which is about from 2 to 4 in the afternoon; the *sry* reigns during the *asal* period, which is about from 4 to 6 in the afternoon; the *barahama* reigns during the *magarib* period, which is about from 6 to 8 in the afternoon; and the *bisnu* reigns on the hour period *aisa*, which is about from 8 in the evening to 6 in the morning. During the following days the cutica rotate in order, until the end of the month, when at the beginning of the new month the *maisuara* again reigns at the *subu* period.

TABLE III.—*Rotation of cutica.*

Hour period.	First day.	Second day.	Third day.	Fourth day.	Fifth day.	Sixth day.
Subu .....	Maisuara .....	Bisnu .....	Barahama .....	Sry .....	Kala .....	Maisuara .....
Lujur .....	Kala .....	Maisuara .....	Bisnu .....	Barahama .....	Sry .....	Kala .....
Asal .....	Sry .....	Kala .....	Maisuara .....	Bisnu .....	Barahama .....	Sry .....
Magarib .....	Barahama .....	Sry .....	Kala .....	Maisuara .....	Bisnu .....	Barahama .....
Aisa .....	Bisnu .....	Barahama .....	Sry .....	Kala .....	Maisuara .....	Bisnu .....

A disease that begins on Sunday, Tuesday, and Saturday has a bad prognosis. A disease that begins on Thursday, Friday, and Monday is of good prognosis. A disease that begins on Wednesday is of neither bad nor good prognosis.

The months have their corresponding prognosis:

TABLE IV.—*Prognosis of months.*

Month.		
First	Mujarram	Bad
Second	Sapar	Do.
Third	Rabi-el-aual	Good
Fourth	Rabi-el-agir	Do.
Fifth	Guiumadil-aual	Do.
Sixth	Guiumadil-agir	Bad
Seventh	Raguiab	Do.
Eighth	Zaban	Good
Ninth	Ramadlán	Do.
Tenth	Xaual	Bad
Eleventh	Chiulcaida	Good
Twelfth	Chiuljiguia	Do.

A disease that begins with high tide is liable to be serious, whereas one that begins with low tide is more likely to be light.

#### TREATMENT OF DISEASES

The treatment of diseases is a mixture of religion, superstition, and medicine concocted by a *tabib* (medicine man) from herbs and plants.

When a person is sick, the windows are not usually closed, but the patient is always kept inside of the mosquito bar, which is made of heavy cloth (coco crudo) for fear the wind may hurt the patient. In some instances a smudge is kept at the foot of the stairs, as the disease is supposed to come up by the stairs, but not through the windows.

The medicine should be of the color of the cutica in which the disease began: maisuara, white; kala, black; sry, several colors; barahama, red; and bisnu, yellow. If the resulting medicine concocted is not of the color of the cutica, the patient

should give the tabib some object, such as money, clothing, turban, etc., of the color of the cutica. Some panditas and tabibs advise also to have the cloth covering the patient, as well as the one covering the medicine and the food, the color corresponding to the cutica in which his disease began.

If on opening the Koran the resulting prognosis of the disease is bad, the patient is moved to another house or place and the Koran is opened anew. The opening of the Koran and the transfer of the patient to another place or house in case of a bad omen is repeated three times or as many times as advised by the pandita.

The following practices are performed according to the advice of the panditas or according to what custom or promise was broken by the patient: (1) *Pedcanduli*, several panditas are invited, who pray to *Alathala* (God) for the healing of the patient, and the family in turn offer food and *sarcá* (alms) to the panditas. (2) *Pagubad*, a form of alligator is made of rice, with eyes made of eggs; it is eaten by the panditas and by the people. This is nearly a constant practice after childbirth. (3) *Paguipat*, in which *culintangan* (music by *culintangs* and *agongs*) is made and food offered by hanging parcels of food wrapped in banana leaves on a branch of a tree or a pole planted near the house. Sometimes a small vinta is made, which is decorated with flags and with canons made of cooked rice and is provided with food and set adrift on the river. (4) *Pedsakay*, which is the same as paguipat, except that a warrior armed with kris and shield dances three times around the pole or branch of tree where the food is hung; then he cuts the tree or pole, and the food is picked up and eaten. (5) *Paigu sa ragat*, which means bathing in the sea of the people around the patient. If the people are far inland where they cannot get any sea water, they use fresh water to which a little salt has been added. The water is placed on a vinta, over which is made a platform where food is placed. The water is sprinkled and squirted on everybody by hand or by a wooden syringe, after which a bath is taken. The patient, however, need not be bathed with salt water, but may be sponged with coconut water to which some leaves of *kilala* and *salimbangan* have been added. (6) *Pandudang*, which is done in cases where sickness is supposed to be due to not fulfilling a promise. A chicken, when cleaned of feathers and viscera, but retaining the head and feet, is boiled in water and placed in a tray, around which gather the patient and his friends, who stick the chicken with knives or bamboo points, repeating words to the effect that the promise is being

fulfilled. (7) *Gatasan*, done in cases where disease is supposed to be due to not fulfilling an oath taken on the Koran. A rope or bejucos is held by the pandita and the patient; on the pandita's end some chickens, clothing, or presents are tied. After a few prayers the pandita severs the rope between them and takes home whatever objects are tied to his end. (8) On the advice of the pandita the patient may promise that should he get well he would make a pilgrimage, *panundiung*, to visit and pray over the grave of a famous person. In all these ceremonies *tutugan* may be added; which is producing smoke by placing leaves of plants or incense over burning charcoal. Dancing by men and women, *bulalacau*, also may take place.

The tabib may be a layman, a pandita, or a hadji who knows how to cure diseases, and the profession is not circumscribed to any definite social class or caste. They are more or less charlatans and enjoy more or less reputation. One of them, Tabib Midsapak, of Maganuy, was famous on account of his success in curing diseases due to the devil.

The tabib or pandita called to attend the sick must leave his house, when called, at the hour period in which the cutica for his social status reigns (maisuara for datus, sry for women, bisnu for panditas, barahama for old patriarchs, and kala for warriors). The tabib, on entering the patient's house, washes his hands and feet up to the elbows and knees, looks at the patient, and concocts the medicine, over which usually he prays a *duana minangung* and afterward blows on it. The following *duana minangung* is the most frequently used around Cotabato:

"Bismil-laji rakmani-r-rajiim. Aljamduli-laji rabil-alamin, ar-rakmani rajlim; malikiyau-midin, iya kana-ambudu, wa iya kana-astain, ij-dinas siru-atal mustakim, siru-atal ladina an-amta ala-ijim, gai-iril maglubi ala-ijim, wa alau-waj lin amin."

#### MEDICINES USED

The pharmacopoeia of the tabib is very extensive and contains plants, herbs, prayers, and cabalistic signs. The Maguindanaos possess books and writings containing prescriptions for diseases, called *paubatan*. Several of these, obtained from Datu Mastura, of Nuling; Datu Mañguda, of Lumbayanagui; Datu Guiukulanu, of Makadalung; and Saika Datu, of Taviran, were examined, and the following recipes are translated from them as illustrations:

*Amenorrhœa*.—The shavings of the bark of the following trees are mixed: *Bunyalawan*, *maguiakani*, *garu*, *saandana*, and *dali-ma*; linseed oil is added, and the concoction is drunk.

*Anorexia.*—An amulet is made with the words illustrated in fig. 2 written on it. This is used for children who do not suck or adults who have no appetite.



FIG. 2. Amulet for anorexia.

*Asthma.*—Write on a white cup the prayer called *patija* or *duana minangung*. In such a cup pomelo juice is placed in which a piece of hard Moro salt has been mixed for a short time. This mixture is then drunk.

*Cold.*—The following is a good medicine for a cold which produces rattling in the throat. Take equal parts of the earthen nest of wasps, shell of a hen's egg that did not hatch, and Chinese face powder, mix together and pulverize in a mortar, add pomelo juice, and apply to the throat.

*Cough.*—The following signs (fig. 3) should be written in a white plate or cup and water placed on it. The water is drunk.

*Crying.*—The following signs (fig. 4) should be written and made into an amulet for a child who cries long and often.

*Disease of children (infantile beriberi?).*—Mix onion, incense, pepper, bearded palay, and any dirt in any crossbeam near the stairway of the house, add three eyelashes and a leaf of nipa from the roof, burn the whole mixture, and smoke the child while repeating the following prayer:

"Kaji ali andu jambri andu aski."

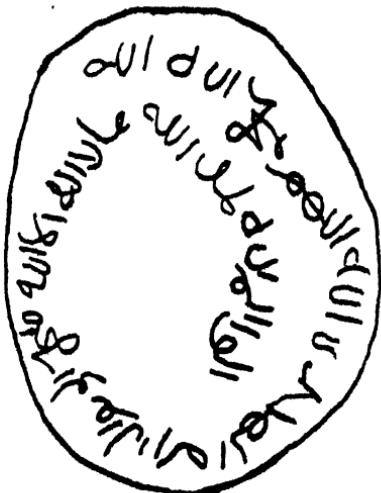


FIG. 3. Amulet for cough.

*Disease of pain due to iblis (devil).*—Chew together some *hubigan*, *kisul*, add onions, and spit on the painful part, then roll a chicken egg over it, while the following prayer is pronounced:

"Alajula ilaja ilajualayu lkayu mututa janunu sinatun ualanu munlaju mapi sampeki uamapil arlle manzaladchi yasepau enlaju elaby isniji alamu mabaena aydijim uamajalpajum ualayujituna bisayninminilmiji ilabimasa auasi-a kursiuju samawate ual arola ualaya uduju ipiujuma uaual aliul alim."

*Disease of men (gonorrhœa).*—Cook together in water fruit of *tungki*, some pepper, saffron, cinnamon, *sibucao*, and *sanki*. This water should be taken at intervals, but should not be taken too much at a time, as it would produce diarrhœa.

*Dysentery.*—Cook together in water shoots of *buri*, *sibucao*, and guava. The water is then drunk.

*Harmful prayers.*—The signs shown in fig. 5, drawn on the door of the house, are a protection against any harmful prayer.

*Headache.*—Obtain *sanki*, leaf of *alem*, fruit of *tunki* and *kisul*, and shoot of a banana called *saguiniga busau*. Make shavings of all of these, add a little water, press them out together, and apply on the head.

*Internal inflammations.*—Obtain equal parts of the bark of the plant *katayatay*, shavings from *sibucao*, and leaves of *sambung*. Crush these together in a mortar and take.

*Malaria.*—Obtain thirty leaves of *salaysina* (yerba buena), on each of them write the letter *alip*, and then rub the body with them. Cook bamboo shoots in water, add a little honey, and then drink the mixture.

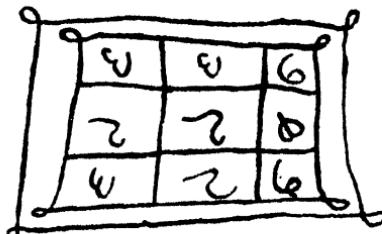


FIG. 4. Amulet for crying.

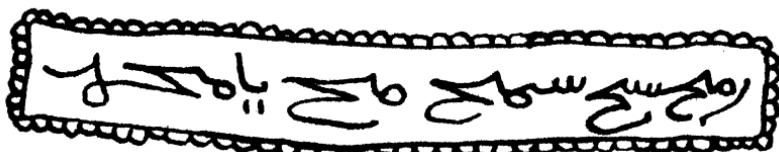


FIG. 5. Amulet for harmful prayers.

*Pain in the abdomen or side.*—Boil in water some garlic, red onions, and seven seeds of pepper. This is to be drunk tepid after saying the following prayer:

"Latud ridikujul absar ua jua yud rik jul absar ua jua latipul jabir."

*Pain in the heart.*—Wrap in a banana leaf about a handful of leaves of tagum and pepper, some ginger and saffron, and a little pomelo juice, place over burning charcoal, and apply on the painful part.

*Pantak (mancuculam).*—Certain signs drawn on a piece of white paper and sewn on the right upper side of the *malung* (sarong) have medicinal qualities and are a preservative against pantak.

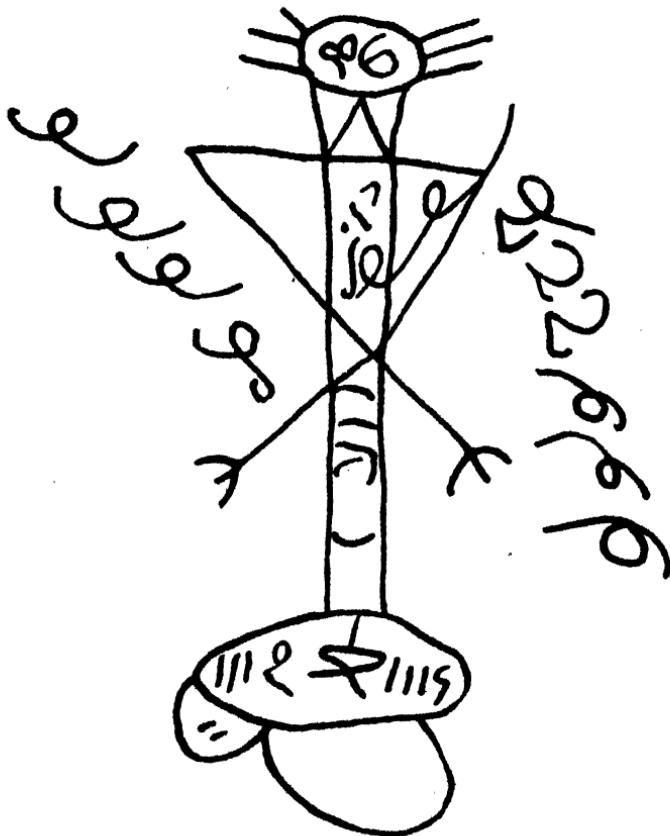


FIG. 6. Amulet for pantak.

*Saitan (Satan).*—The signs shown in fig. 7 have medicinal qualities and are a preservative against satanic diseases brought on by the air. They are drawn on the painful part.



FIG. 7. Amulet for saitan.

*Stomach ache, acute.*—Saffron, ginger, and *tikuas* in equal parts mixed with burnt *kalamungui* and juice of lemon. The mixture is rubbed on the abdomen without adding water.

*Stomach ache with vomiting.*—Mix, add vinegar, and drink the following: *lubigan*, *cogon*, *buyo*, *kisul*, ginger, and pepper.

*Spitting blood.*—*Buñgalauan* and coral powder well mixed with a little water, to be taken after praying the *duana minangung*.

*Vomiting blood.*—Write in a white plate the following:

"Audubilaji biisaki ualkudaraki minsain malaju jad an sua jaalaju ilaju uala ilaja ila laju ua kad pajamata ku naka." Water is then placed in the dish and drunk.

Besides the medicines mentioned in the above prescriptions, the following plants have medical reputations:

*Bagú.*—*Bagú* is a small tree growing in the forest. . The leaves are macerated in water and applied on the abdomen and temporal regions in cases of fever.

*Baricacab.*—*Baricacab* is a plant whose bark is very bitter, from which a decoction is made in cases of intentional abortion.

*Bubug.*—*Bubug* is a tree with very bitter bark. It is used by women in intentional abortions.

*Gusan.*—*Gusan* is a grass somewhat similar to sugar cane. It grows in the forest. The tender sprouts are boiled in water and drunk in cases of fever.

*Lalasabay.*—*Lalasabay* is a plant with leaves similar to the *sambung*. It has the reputation of curing the enlargement of the spleen due to malaria.

*Patauali (macabuhay).*—This is a creeping forest plant. A decoction is made which is very bitter and is used as a drink for fever.

*Tanγan-tanγan.*—This is the castor-oil plant. The leaves are used to apply on the ears in cases of earache.

## SURGERY AND TREATMENT OF WOUNDS

No surgery is performed by the Maguindanaos. Even in treating an abscess, they ripen it by means of hot water or fomentation of some kind or other; and when it is ripe, the point is opened and tobacco or fine shavings of stalk of coconut is applied to drain the pus.

The following prescription for inflammation or swelling are translated from a *paubatan*:

1. A small amount of rice is toasted brown and pulverized. Mix some saffron, add a little salt and pomelo juice, and apply on the swelling.

2. Crush tender leaves of *lagundi*, mix with a little pomelo juice, and apply on the swelling.

3. Burn the stalk of a mongo tree, pulverize, mix a little wine, warm it up a little, and apply.

In some cases of pain and inflammation wet cupping is resorted to. Several incisions are made on the skin, and then blood is sucked through a horn.

In the treatment of wounds, they use the following means:

1. Kerosene and bandaging with rag.

2. *Tudi* (*caturay*). *Tudi* is a tree with white flowers that are used as salad by Filipinos and Spaniards. Fine shavings are made of the bark and wood, and the juice is applied to the wound.

3. Salt, lime, and oil, equal parts, cooked together and applied.

4. *Tingan*, or *tigba* grass. The tender trunk is crushed, and the juice is applied.

The Maguindanaos have no idea of infection and seem to think that pus is a natural secretion of the wound.

## MANAGEMENT OF LABOR

The midwife, called *ualian*, helps in the management of labor. A man or another woman pushes the uterus down through the abdominal walls. A pandita prays and blows on the abdomen. The *ualian*, the helpers, and pandita wash their hands and feet before approaching the patient.

When the labor pains begin, the patient is placed in bed, and the *ualian* washes the vulva of the woman with water to which bark of *bunduy* (a tree with white flowers) and *karumunigan* (a kind of grass) have been placed. No further manipulation is necessary, except a gentle massage of the abdomen and a rag held on the anus, but not on the vulva. During the second

stage the expulsion of the child is helped by pushing the uterus down. After the completion of the labor, the uterus is massaged in an upward direction to return it in place.

When the baby is born, the cord is not cut at once, but is allowed to remain until the placenta is expelled. Then the child and placenta are washed with cold water, and after this the cord is extended up to the ear and cut at this level and wrapped with a rag. The cord must be cut with a bamboo knife, because a steel knife is liable to cause pain and inflammation. A steel knife could be used in case of emergency. No medicine is placed at the cut end of the cord.

In a few days the cord falls off, and it is hung on the hammock of the baby. When the baby suffers stomach ache, this dry cord is placed in a cup of water, and the water is given to the child to drink. When the child is older, the dry cord is given him to use as *haguimat* (anting-anting) to be wrapped up in his belt, when he travels to distant places.

The child is not given colostrum to suck, as it would give him stomach ache; it is bathed every day and allowed to go naked.

The mother is allowed to get up after childbirth, and a string is placed loosely around the waist.

If the baby cannot be born, no operative interference is made nor external violence performed, but prayer is offered by the panditas and hadjis.

At the time of quickening during pregnancy *kilidin* is performed, which consists of manipulations by a midwife to straighten the position of the child. This is always performed in cases of primipara, when panditas and relatives of the husband and wife are gathered and other ceremonies are performed, such as, praying, sprinkling the husband and wife with coconut water, etc.

#### DENTISTRY

The Maguindanaos know how to pull and medicate carious teeth. For a carious tooth they apply ginger and salt heated together and placed while hot in the hole of the tooth.

They do not make any bridge work, but they can put on crowns of silver and gold. One often sees around Cotabato Moros with gold front teeth. These are made by Maguindanao silversmiths and consist of a body of silver that ends at the base in a nail that fits into the pulp cavity, and over the labial surface a thin plate of gold is soldered. The root is prepared by cutting the tooth at the neck. The pulp is allowed to decay, and after a few days it is removed with a nail or wire and the false tooth

is fitted into the canal, but as no dental cement is used, the tooth could be removed at will.

#### PREVENTION OF DISEASES

The transmission of communicable diseases is favored by conditions similar to those found in the Christian provinces, such as ignorance of the people, unhygienic surroundings, poor nutrition, eating with the fingers, and frequency of travel; however, there are two customs peculiar to the Mohammedan population of Cotabato that add to the means of transmission, such as the habit of washing the genitals after an act of nature and the ceremonies in connection with the dead.

The habit of washing the genitals after an act of nature being sort of a religious mandate, all Moros live on the bank of rivers and streams, as they do not dig wells, and they must defecate or urinate in the water in order to wash properly.

When a Moro dies, all the panditas in the neighborhood and from great distances, if the dead is important, gather around, although uninvited, to offer prayers and get their fees. The corpse is washed very thoroughly by a pandita called *manustican*, special attention being paid to the natural orifices, the abdomen being massaged to press out the remnants of urine and faeces; if faeces do not come out, a finger is introduced into the anus. Then the corpse is wrapped in a white cloth and held in the arms of two or four panditas, *mapasalay*, while the highest pandita present administers the nine kinds of baths prescribed by the Koran.

The Maguindanaos know that chicken pox and measles are contagious, but do not take any means to prevent their spread. In cases of severe epidemics of smallpox some people escape to the forests and hills, but as a general rule they take no precautions.

There is no vaccination performed by the Maguindanaos comparable to vaccinations from pus of true smallpox as performed by Moros in Jolo.

Cases of leprosy are isolated, and the patients are placed in houses away from the community.

In some instances white flags are placed in the houses to prevent the entrance of epidemics, as noted during the cholera of 1915.

## ILLUSTRATIONS

### PLATE I

- FIG. 1. One page of a paubatan (Moro medical book), written by Datu Manguda Ibad.  
2. Two facing pages of a paubatan (Moro medical book), written by Saika Datu sa Tavidan.

### TEXT FIGURES

- FIG. 1. The smaller end of the egg.  
2. Amulet for anorexia.  
3. Amulet for cough.  
4. Amulet for crying.  
5. Amulet for harmful prayers.  
6. Amulet for pantak.  
7. Amulet for saitan.



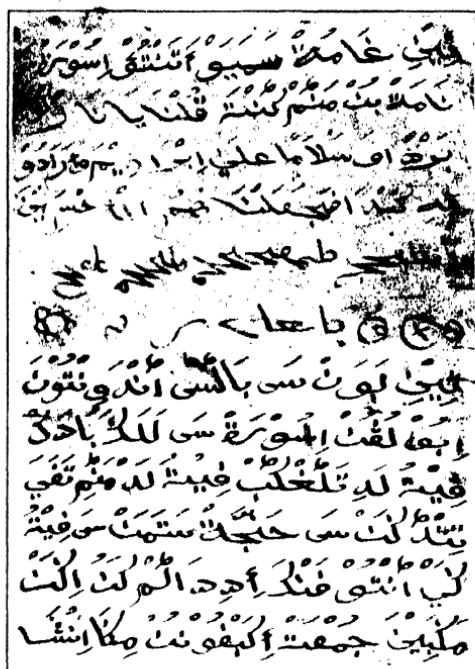
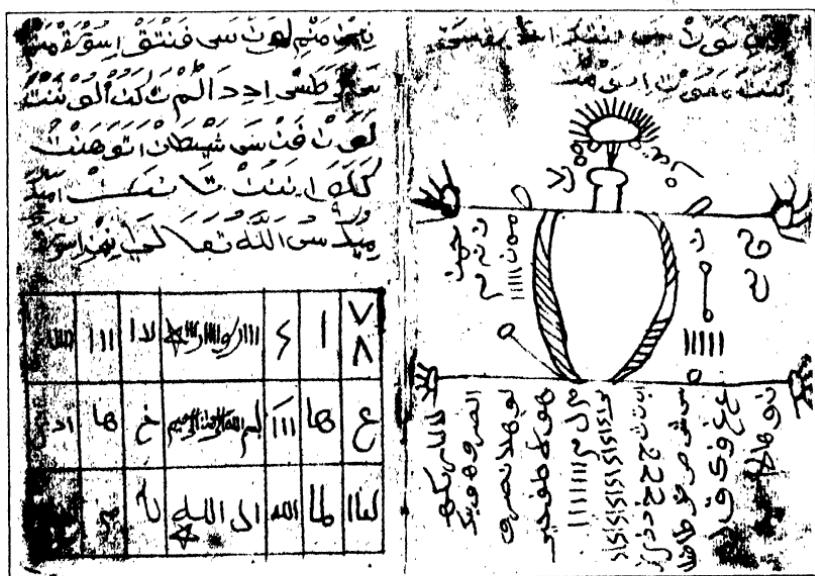


Fig. 1. One page of a paubatan (Moro medical book), written by Datu Manguda Ibad.



**Fig. 2.** Two facing pages of a paubatan (Moro medical book), written by Saika Datu sa Tavidan.



## A DISEASE IN CATTLE IN THE PHILIPPINE ISLANDS SIMILAR TO THAT CAUSED BY ANAPLASMA MARGINALE THEILER<sup>1</sup>

By WILLIAM HUTCHINS BOYNTON

(From the Bureau of Agriculture, Manila)

THREE PLATES AND ONE TEXT FIGURE

The animals in which this disease was found were native cattle from Batan Island, which is located some 48 kilometers from the northern coast of Luzon. As rinderpest has not been introduced on that island and as the animals from there are highly susceptible to that disease, these cattle are used at the Veterinary Research Laboratory for experimental work on rinderpest.

The animals that were used in the experiments recorded in this paper arrived in Manila by boat from Batan Island on June 7, 1915. They were placed in a corral in Manila until June 19, when they were purchased by the veterinary division, Bureau of Agriculture, for experimental purposes; brought to the Veterinary Research Laboratory at Pandacan on the afternoon of June 19; and placed in quarantine with several other animals. Their temperature was taken twice each day, and their general appearance was noted.

On the morning of July 12, 1915, cow 3929 showed a temperature of 38.6° C. The average temperature for fourteen other cattle kept in the same shed and under similar conditions was 37.8° C. The afternoon temperature of this animal was 39.6° C. Bull 3932 also showed a temperature of 39.7° C. Although these temperatures were higher than those of the other animals, they were not high enough to cause rinderpest to be suspected. Their blood was examined for surra in moist preparations and found negative. This was thirty-five days after arriving from Batan Island and twenty-three days after being brought to the laboratory. On July 13 both of the above animals showed temperatures of over 40° C.; they were immediately taken out of the quarantine shed and placed in the shed with sick animals. Their blood was again examined for surra with negative findings.

On July 15, 1915, bull 3939, which was in the quarantine shed,

<sup>1</sup> Published in *Phil. Agr. Rev.* (1917), 10, 119-127.

showed a morning temperature of 38.8° C. and an afternoon temperature of 40.8° C. This animal was immediately removed and was placed with the sick animals. Its blood was also examined for surra with negative findings.

On July 15, 1915, cow 3929 refused food and had a depressed appearance. On July 16 this animal presented a very depressed appearance, but remained standing and spread its legs as if trying to brace itself to keep from falling; the pulse was 106 per minute; its body was covered with flies, which it made no effort to drive away (Plate I, fig. 1). Since surra could not be found and the animal did not present the clinical picture of rinderpest, further blood examinations were made, and at this time bodies similar to *Anaplasma marginale* were located, about 30 per cent of the red corpuscles being infected.

On July 17 the animal was in a stupor; the respiration was slow and sonorous. It remained standing with its legs spread and its body leaning against the stall. It appeared to lose consciousness with its eyes open and would start to fall, but would recover itself (Plate I, fig. 2). The pulse was 98 per minute and wiry, and pronounced œdema was present under the jaw. The animal was covered with flies, which it made no effort to drive away. There was practically no response on trying to rouse the animal. On the afternoon of the 17th its temperature was 37.4° C., which is subnormal. As it was feared the animal would die during the night and as it was desired to perform the autopsy while the body was in a fresh condition, the animal was led out and killed. When led, it was very weak, moved with great difficulty, and had to be helped by a man on either side to keep it from falling; when standing, it did not need any assistance, as it kept its legs well spread for support (Plate I, fig. 3).

Upon autopsy the blood was found to be very anæmic, having the appearance of slightly hæmolyzed blood. All the visible mucous membranes were pale. There were epicardial hemorrhages at the apex of the heart. The endocardium was pale and bluish, and there was a light red clot in both ventricles. The flesh, in general, was pale and bloodless. The lungs were distended and very pale.

A marked gelatinous infiltration was present, extending along the upper part of the throat and under the lower jaw.

Practically all the lymphatics were swollen and œdematosus, exuding a watery serous material upon section. The fat covering the omentum and around the intestines was yellow, as if discolored with bile. The gall bladder was markedly distended,

containing thick green bile almost of the consistency of jam. The liver was brownish yellow, with heavier yellow streaks in places. It was also very friable, but was not enlarged to any noticeable extent.

The spleen was enlarged to one half again its normal size, and the pulp was soft and bulged out on the cut surface upon section.

The kidneys were congested and presented a rather blotchy appearance. The blotches were lighter than the general substance of the organ.

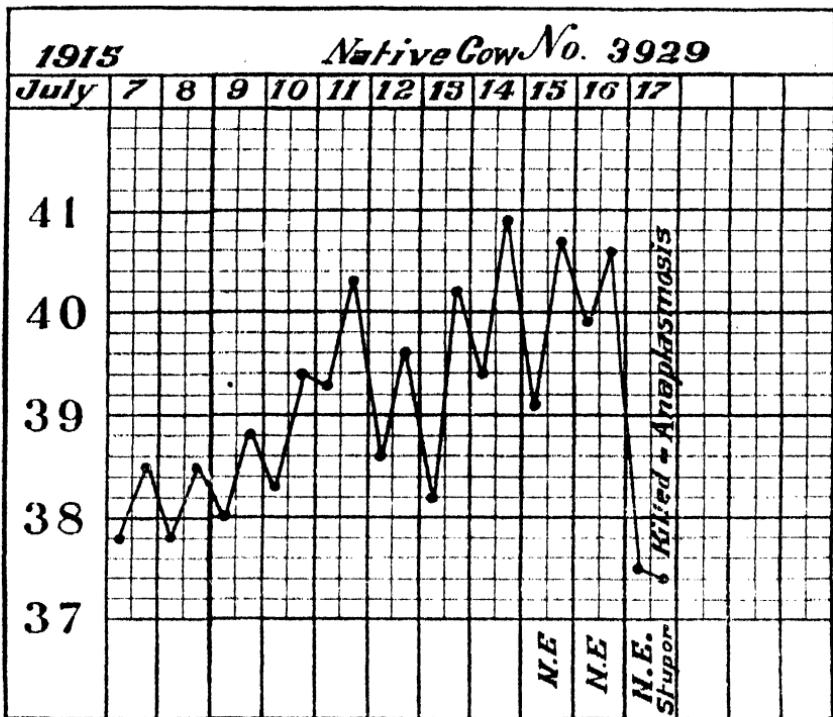


FIG. 1. Temperature chart of cow 3929.

The intestines were streaked with bile their entire length. The faeces in the large bowel were hard and in some places covered with mucus. The fourth stomach contained watery bile-stained faecal matter; the mucous membrane was slate-colored, and as far as could be noticed contained no hemorrhagic or congested area.

The throat and region of the fauces were free from erosions or congestion.

The entire intestinal tract, except for being bile-stained, was slate-colored. The urinary bladder was markedly distended and

contained slightly turbid yellowish brown urine. No signs of blood or haemoglobin were in evidence. The general appearance was that of marked anaemia.

Tissues were taken from the heart, spleen, lungs, liver, kidney, fourth stomach, and duodenum. These were fixed in sublimate acetic acid and sectioned.

Five cubic centimeters of heart's blood were immediately taken from cow 3929 and injected subcutaneously into bull 3926. The latter animal was kept under observation until February 29, 1916, and never showed any ill effects from the injection, nor were anaplasmatlike bodies ever found in its blood.

Bulls 3932 and 3939 showed a few anaplasmatlike bodies in their blood, ranging from 2 to 3 per cent, but both contracted rinderpest after their removal from the quarantine shed and died of that disease.

The blood-smear preparations and sections of tissue were stained with Giemsa's, Wright's, Jenner's, and Hastings's stains. The best pictures were procured with Giemsa's following the technic used by Sieber.(5)

Cover glasses have to be cleaned well in alcohol, then a thin film of blood is spread on, and, with the smeared side downwards, they are thrown into hot sublimate alcohol (concentrated watery sublimate lotion two parts, alcohol one part). The preparations remain in this solution for two to twenty-four hours. Then they are taken out with small horn forceps, well rinsed, and, in order to remove the sublimate, thrown into a solution of 2 per cent iodide of potash (100 parts) and Lugol's solution (3 parts); rinsed again after ten to fifteen minutes, and in order to remove the iodine put into a watery solution of sodium hyposulphite (0.5 per cent). The preparations having become colorless by the solution of iodine (after five to ten minutes) are now carefully rinsed in water and fit for other staining manipulations. \* \* \*

For Giemsa staining of the above-mentioned smears, diluted Giemsa lotion is used ( $\frac{1}{2}$  to 1 drop in 1 ccm. aq. dist.). This liquid has to be changed several times during the first two hours, then the preparations are left in the solution for four to twenty-four hours. Then they are well rinsed and brought through the following:

Xylol 5, acetone 95.

Xylol 30, acetone 70.

Xylol 70, acetone 30.

Xylol pure.

According to the degree of differentiation, the preparations are left for a longer or shorter time in the acetone liquids. The preparations are taken out of the pure xylol and placed at once in oil of cedarwood (not Canada balsam).

This method was slightly modified by using 1 to 1,000 potassium carbonate solution instead of the distilled water in making up the stain. This causes the preparations to stain deeper.

**MICROSCOPIC PICTURE OF THE BLOOD (PLATES II AND III)**

As was stated, the blood was very anæmic, which made it difficult to obtain good, even smear preparations.

In stained preparations the red cells were lacking in haemoglobin and had a great tendency to become crenate, irrespective of the precautions taken to prevent this. As a rule, the bodies were situated on the margins of the corpuscles. In some instances they protruded over or at least caused the corpuscle to bulge from the margin. Where two bodies were present in one corpuscle, frequently one was situated on the periphery, while the other would be nearer the center, in the center, or beyond the center; in some instances they would be on the periphery of the corpuscle, one on either side. This indicates that frequently after division one of the newly formed bodies remains at or near its original location, while the other migrates to the other side of the corpuscle. In other cases they divide, and both remain at the periphery on the same side of the corpuscle.

Frequently the newly formed bodies after division are of equal size; however, the reverse is common in which one may be much larger than the other. A few instances were noted where division was not complete, one being as much as three times the size of the other, the smaller giving the appearance of a bud protruding from the larger, similar to the condition noticed in yeast cells undergoing multiplication.

As a rule, one or two bodies were found in an infected cell, but four or even five in a cell were not of rare occurrence.

With Giemsa's stain the bodies become a purplish red, staining very brilliantly, and are easy to distinguish. They vary in size from 0.5 micron to 1.5 microns.

They stained uniformly and appeared to be composed of a mass of chromatin with no cellular substance. A slight halo is present around a majority of the bodies, which may be due to the lack of haemoglobin in their immediate vicinity, but this halo does not have the appearance of a lighter staining body substance.

With Wright's stain the bodies appear smaller than with Giemsa's method. It may be possible that with Wright's method all the chromatin is not stained; however, a body structure could not be distinguished.

Morphologically they are spherical or have a slightly uneven border, thus making any definite shape impossible, but there is a general tendency toward being spherical. Undoubtedly

their shape depends considerably upon the stage of development. If they are fully developed and have not reached the stage for apparent reproduction, they are spherical and have a smooth border. When they reach the stage for multiplication, either equal or unequal fission takes place, thus breaking the evenness of the contours and distorting the spherical shape. They may assume slightly triangular, slightly oval, or various uneven, spherelike shapes. Those recently divided are, as a rule, spherical.

Theiler, (7) in his extensive work on anaplasma, states that *Anaplasma marginale* is transmissible only in blood containing corpuscles, as the organisms have lost their body plasma—for which reason they derive their generic name—and have to exist in the cell protoplasm, making them a strictly intercellular organism. He failed to produce the disease by injecting filtered blood, proving that there was not a stage in the development of the organism which was filterable.

He also shows that the incubation period after the injections of blood containing anaplasma depends upon two conditions. If the amount of blood is large, the incubation period is shortened, and if the strain has been passed through several animals by injection, the same result obtains. He finds this period to average between sixteen and forty days, usually in the neighborhood of from twenty-three to twenty-five days.

He distinguishes two varieties of anaplasma, depending upon their location in the red blood cells, the severity of the disease, and the inability of one to confer complete immunity upon the other. *Anaplasma marginale* is located upon or near the periphery of the cell, and the other *A. marginale* (variety *centrale*) is somewhat small and is located near to, or in, the center of the corpuscle. It has not been noticed that *A. centrale* causes death either by direct inoculation of blood or by tick infestation, while animals affected with *A. marginale* frequently succumb. An animal recovering from *A. centrale* infection, when inoculated with the *marginale* variety, develops the disease, but in a much milder form than would be otherwise encountered, which proves that although there is not a complete immunity there is some protection provided.

The incubation period for this disease after tick infection is rather long and has a wide range, varying from a few days under two months to a few days over three months.

Animals that were immune to *Babesia bigemina* could be infected with anaplasmosis either by means of ticks or by blood inoculation, which proved that *B. bigemina* afforded no

immunity against anaplasmosis. In further experiments Theiler proved that animals recovering from anaplasma infection were not immune to *B. bigemina* either by means of ticks or by blood inoculation. He suggests that in inoculating with *B. bigemina* for the purpose of immunization it is just as well to inoculate with anaplasma at the same time. The inoculation period of *B. bigemina* is so much shorter, that the animal will have ample time to recover before the anaplasma reaction takes place.

He has also proved that animals recovering from *Babesia bigemina* and anaplasmosis can be easily infected with *Babesia mutans*, which shows that no immunity is conferred either separately or together against *B. mutans*.

Theiler proves that two varieties of tick can transmit the disease: *Boophilus decoloratus*, the blue tick, which also transmits *Babesia bigemina*, and the black-pitted tick, *Rhipicephalus simus*.

Frequently a double infection of *Anaplasma marginale* and *A. centrale* is found in the same animal, this being especially true after tick infections.

The three cases herein mentioned are the only ones which have come to any notice during the past twenty months. Further developments of the disease have been awaited, in order to obtain a better insight concerning its etiology, modes of infection, pathology, etc., but with no success, which leaves this paper merely a narrative discussing three cases that gave pictures similar to those described by Theiler and by Sieber as anaplasma infection. This creates a doubt as to whether that disease really exists in the Philippine Islands, or whether these animals suffered from some other ailment which brought about the formation of these anaplasmalike bodies in the red blood cells.

On studying the literature, it is found that bodies similar to anaplasma may be produced artificially. Very creditable work has been done by Dias and Aragao,<sup>(2)</sup> in which instance they were able to produce anaplasmalike bodies in dogs, rabbits, and guinea pigs by injecting them subcutaneously with small doses of phenylhydrazine. They were also able to produce a similar condition in rabbits by injecting them subcutaneously with small doses of nitrobenzol, a similar condition in dogs by injecting them subcutaneously with small doses of pyrogallic acid, and a similar condition in calves by injecting them with a series of fairly large doses of trypan blue.

In considering these results, there arises a doubt as to whether this was the infectious disease designated by Theiler as anaplasmosis, or whether it was the result of some other infectious or noninfectious disorder from which the above-mentioned an-

imals may have been suffering, thus causing the formation of these bodies in their red blood cells.

Porter(4) has observed anaplasmalike bodies in the red blood cells of mice, canaries, swallows, martins, lizards, snakes, frogs, toads, and sticklebacks, which are representatives of all the great groups of the vertebrates. These bodies were most prevalent in animals that were anæmic.

Balfour(1) has found anaplasmosis in sick donkeys from Malakas on the White Nile and is led to believe they are true protozoan parasites.

Spreull(6) has also observed the marginal points in the blood of cattle in South Africa and declares his conviction that the marginal points are parasitic in nature.

Jowett(3) observed marginal points in the red blood cells of a cat that had been inoculated with a trypanosome infecting cattle in Cape Town, South Africa. This cat was suckling a kitten at the time, and similar bodies were found in the blood of the kitten. He also found similar bodies in the blood of rats infected with this trypanosome and noticed them in the blood of apparently healthy noninfected rats. He also states that—

In the case of the trypanosome-infected, and consequently anæmic, subjects (both cats and rats) the bodies were, as a rule, more numerously present than in other animals which appeared healthy and which had not formed the subject of experiment. They were sometimes markedly noticeable in the blood cells of our experimental rats the day following the administration of a dose of antimony.

Jowett quotes Bruce, Hammerton, Bateman, and Mackie as having noted the occurrence of marginal points in cattle (especially calves) in Uganda. These investigators refer to these bodies in the following terms:

If these bodies really constitute a new and undescribed parasite, the discovery will be one of great interest. Bodies similar in every way to these are found, however, in healthy young rats, goats, calves, etc., so that it is difficult to believe at once in their parasitic nature. Rather would they appear to be cell inclosures due to rapid changes taking place in the blood, such as takes place in young animals or in anæmias.

#### CONCLUSIONS

1. Cattle 3929, 3932, and 3939 presented bodies in their red blood cells similar to *Anaplasma marginale* as described by Theiler and by Sieber.
2. Cow 3929 presented the symptoms and lesions of anaplasmosis as described by Theiler and by Sieber.
3. The heart's blood of cow 3929 was injected subcutaneously

into supposedly susceptible bull 3926. The blood had no demonstrable effect either physically or by blood examination upon this animal during a period of two hundred twenty-six days.

4. From the results obtained by various investigators and from the results herein cited, nothing definite can be stated as to whether there is an actual infectious disease caused by a protozoan microorganism which Theiler classifies as anaplasma or whether these marginal points are merely secondary effects from various conditions.

5. There is a possibility that there is an infectious disease caused by anaplasma, and that there are bodies formed in the red blood cells from various other conditions which are so similar in appearance and staining reaction to anaplasma that they cannot be differentiated at the present time.

#### REFERENCES

1. BALFOUR, A. Anaplasmosis in donkeys, *Journ. Comp. Path. & Therap.* (1911), 24, 44-47.
2. DIAS, C. E., and ARAGAO, H. DE B. Pesquisas sobre a natureza dos anaplasmas, *Mem. Inst. Oswaldo Cruz* (1914), 6, 231-249; 2 plates. (See also *Brazil Medico*, April 22, 1913.)
3. JOWETT, W. Some observations on the subject of marginal points, *Journ. Comp. Path. & Therap.* (1911), 24, 40-44.
4. PORTER, ANNIE. On anaplasma-like bodies in the blood of vertebrates, *Ann. Trop. Med. & Parasit.* (1915), 9, 561-568.
5. SIEBER, HANS. *Anaplasma marginale* (Theiler). *Rep. Gov. Vet. Bac., Dept. Agr., Union of South Africa* (1909-10), 104-116; 5 plates.
6. SPREULL, J. "Marginal points" or a new intracorporeal parasite in the blood of cattle in South Africa, *Journ. Comp. Path. & Therap.* (1909), 22, 354-357.
7. THEILER, A. Further investigations into anaplasmosis of South African cattle, *First Rep. Director Vet. Research, Dept. Agr., Union of South Africa* (August, 1911), 7-46.



## ILLUSTRATIONS

[Plates loaned by the Bureau of Agriculture.]

### PLATE I

- FIG. 1. Cow 3929 leaning against the stall, with legs spread to keep her from falling. Last stages of questionable anaplasmosis.
2. Cow 3929 in a semicomatose condition, respiration sonorous, pulse wiry, body covered with flies, legs spread to keep her from falling. Last stages of questionable anaplasmosis.
3. Cow 3929 just before being slaughtered, body covered with flies, legs spread, œdema under jaw and throat. Animal had a subnormal temperature. Last stages of questionable anaplasmosis.

### PLATE II

- FIG. 1. Two red blood cells containing anaplasmalike bodies: (a') *marginal* type (Theiler); (b') *centrale* type (Theiler). Notice the halos around the bodies.
2. Two red blood cells containing anaplasmalike bodies: (a') *marginal* type (Theiler), protruding slightly beyond the periphery of the cell; (b') two bodies apparently shortly after division, one remaining on the margin and the other migrating across the cell.
3. A red blood cell containing a body which has almost completed division. Notice the halo around the bodies.

### PLATE III

- FIG. 1. Two red blood cells containing anaplasmalike bodies: (A) containing two bodies undergoing division; (a') body becoming oval before division takes place; (a'') one body much larger than the other, division almost complete, giving the appearance of budding; (B) two bodies in a cell, both remaining at the margin.
2. A red blood cell containing three anaplasmalike bodies of varying size, giving the extremes in size ordinarily noticed.
3. A red blood cell containing four anaplasmalike bodies, two showing unequal division, and two showing equal division.

### TEXT FIGURE

- FIG. 1. Temperature chart of cow 3929.





Fig. 1. Cow 3929 leaning against the stall, with legs spread to keep her from falling. Last stages of questionable anaplasmosis.



Fig. 2. Cow 3929 in a semicomatose condition, respiration sonorous, pulse wiry, body covered with flies, legs spread to keep her from falling. Last stages of questionable anaplasmosis.



Fig. 3. Cow 3929 just before being slaughtered, body covered with flies, legs spread, oedema under jaw and throat. Animal had a subnormal temperature. Last stages of questionable anaplasmosis.



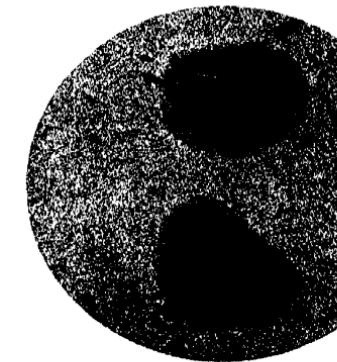


Fig. 1. Two red blood cells containing anaplasmatike bodies: (a') marginale type (Theiler); (b') centrate type (Theiler). Notice the halos around the bodies.

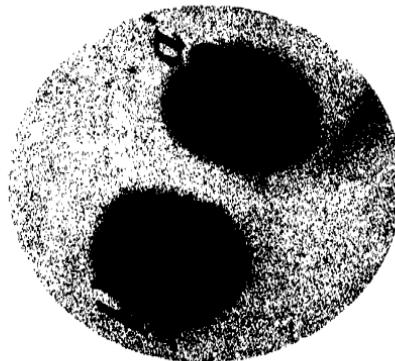


Fig. 2. Two red blood cells containing anaplasmatike bodies: (a') marginale type (Theiler), protruding slightly beyond the periphery of the cell; (b) two bodies apparently shortly after division, one remaining on the margin, and the other migrating across the cell.

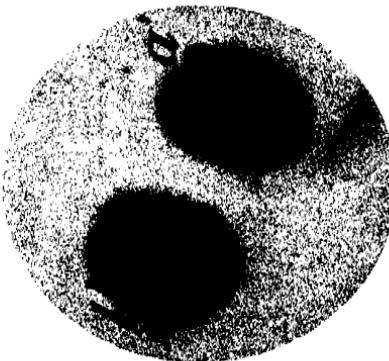


Fig. 3. A red blood cell containing a body which has almost completed division. Notice the halo around the bodies.

PLATE II.





Fig. 1. Two red blood cells containing anaplasma-like bodies: (A) containing two bodies undergoing division; ( $\alpha'$ ) body becoming oral before division takes place; ( $\alpha''$ ) one body much larger than the other, division almost complete, giving the appearance of budding; (B) two bodies in a cell, both remaining at the margin.

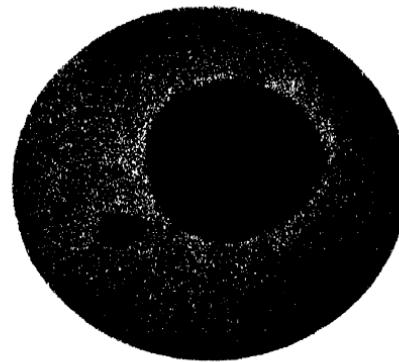


Fig. 2. A red blood cell containing three anaplasma-like bodies of varying size, giving the extremes in size ordinarily noticed.

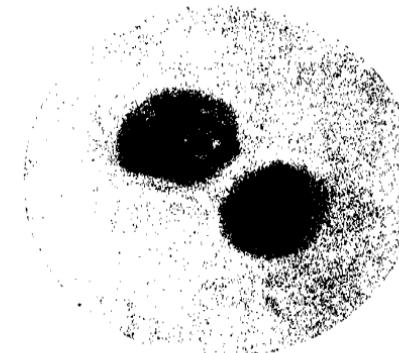


Fig. 3. A red blood cell containing four anaplasma-like bodies, two showing unequal division, and two showing equal division.

PLATE III.



## PROCEEDINGS OF THE MANILA MEDICAL SOCIETY

REGULAR MONTHLY MEETING, OCTOBER 1, 1917

### MINUTES OF THE MANILA MEDICAL SOCIETY

The meeting was held in the College of Medicine and Surgery on the evening of October 1, 1917, President Ruth presiding. There were 16 members present and 2 visitors.

The meeting was called to order at 8.45 o'clock. In the absence of the secretary-treasurer, the chair appointed Doctor Gibson as secretary *pro tempore*.

The minutes of the previous meeting were read and approved.

The council recommended the acceptance of Dr. Frank W. Vincent's application for membership. On motion, duly seconded, Doctor Vincent was elected to membership in the society.

There being no other business, the program for the evening was carried out, after which the society adjourned at 10.15 o'clock.

R. B. GIBSON,  
*Secretary pro tempore,*  
*Manila Medical Society.*

### SCIENTIFIC PROGRAM

#### OBSERVATIONS ON THE INCIDENCE OF INTESTINAL SPIROCHAETES IN THE PHILIPPINE ISLANDS

By DR. B. C. CROWELL AND PROF. F. G. HAUGHWOUT

The authors presented the results of the examination of the stools of 46 persons undergoing treatment for various ailments in the Philippine General Hospital. Of these persons 73 per cent were found to harbor intestinal spirochaetes. The spirochaetal infections bore no apparent relation to concomitant infections with protozoa and helminths. The spirochaetes varied in size from 2  $\mu$  up to a single individual that measured 13  $\mu$ . The apex of the biometric curve stood at 4  $\mu$ .

The paper constituted a preliminary report on more extended work on the subject, with a view to discover if the spirochaetes in association with endamebae may not cause lesions that will respond to treatment with salvarsan, it being pointed out that

some cases of intestinal amœbiasis that are refractory to other forms of treatment do respond to treatment with salvarsan.

The paper included a citation of the more important literature on intestinal spirochætes. The authors do not take up the systematic position of the spirochæte seen by them, nor do they attempt at this time to establish its identity with *Spirochæta eurygyrata* Werner, emend. Fatham. The paper was accompanied by the demonstration of stained preparations of the spirochætes by the hæmatoxylin and Benian's methods.

#### DEMONSTRATION OF OSSIFICATION CENTERS IN THE HUMAN EMBRYO

By DR. EDWARD S. RUTH

The method for demonstrating the formation and ossification centers of bones was first described by Schultze. Human embryos up to the sixth and seventh month of intrauterine development may be used for the demonstration of bone formation. The embryo is first placed in 95 per cent and later in absolute alcohol until the soft parts have all shriveled. The specimen is then placed in a 1 per cent solution of potassium hydroxide until the soft tissues are transparent and the calcareous matter can be distinctly seen. Formalin-hardened specimens may be also cleared in this manner, providing a stronger solution of potassium hydroxide is used, up to 10 per cent. After the embryo is fairly transparent, it is placed in a solution consisting of water, 20 parts; glycerol, 20 parts; and strong ammonia water, 30 parts. In this solution it can be left indefinitely, until the specimen is perfectly clear. For permanent mounting it may be placed in glycerol or it may be prepared according to the Bardeen method, that is, splitting the embryo in the saggital plane and mounting it on a glass plate covered with gelatin; this is then placed in a solution of glycerol, which hardens the gelatin by dehydration and fixes the specimen to the glass plate.

A number of human, pig, and duck embryos, which were prepared by the above method, were demonstrated. The human embryos varied from 2 months and 1 week to 4 months and 3 weeks of age.

#### ACIDOSIS AND THE DETERMINATION OF THE CARBON DIOXIDE OF THE ALVEOLAR AIR

By DR. R. B. GIBSON

The various recently proposed methods<sup>1</sup> for determining the alkaline reserve of the body were discussed, in particular the

<sup>1</sup> Marriott, Van Slyke, and others.

determination of the carbon dioxide of the alveolar air and its limitations. Emphasis was placed on the practicability for clinicians of the colorimetric methods for the carbon dioxide of alveolar air, the indicator method for the hydrogen ion content of the blood, and the titratable acidity plus the fixed ammonia of the urine as an index of acidosis. A simple test and treatment suggested by L. J. Henderson, depending upon the administration of sodium bicarbonate until a urine amphoteric to litmus is obtained, was referred to also. No original observations were presented.

R. B. GIBSON,  
*Editor of the Proceedings,*  
*Manila Medical Society.*

#### MINUTES OF THE PHILIPPINE ISLANDS MEDICAL ASSOCIATION

A business meeting of the Philippine Islands Medical Association was called to order by President Crowell at 10.15 o'clock in the College of Medicine and Surgery immediately following the adjournment of the Manila Medical Society, for the purpose of electing a second vice president and 3 councilors.

The minutes of the previous business meeting were read and adopted.

The resignation of Colonel C. J. Manly as councilor for two years was accepted with regret. The president stated that the positions of second vice president and councilor for one year were vacant, because of the departure of Doctors Keating and Hillman from the Philippine Islands. The councilor for five years was not elected at the previous meeting. The chair appointed a nominating committee of Doctors Schöbl, Johnston, and de la Paz.

It being moved, seconded, and carried that the association proceed to the election of the above-mentioned officers, the report of the nominating committee was presented as follows:

For Second Vice President:	Dr. Fernando Calderon
For Councilor for five years:	Dr. John A. Johnston
For Councilor for two years:	Dr. Frank W. Vincent
For Councilor for one year:	Dr. Potenciano Guazon.

There being no further nominations, it was moved, seconded, and carried that the secretary cast the unanimous vote of the association for the above nominees.

The president then outlined the proposed plans of the council to hold the next scientific session jointly with the Colegio Médico-Farmacéutico de Filipinas, stating that the approval of the sec-

retary of the American Medical Association had been obtained by the secretary-treasurer for such a meeting.

There being no other business, the association adjourned at 10.45 o'clock.

R. B. GIBSON,  
*Secretary-Treasurer,*  
*Philippine Islands Medical Association.*

# INDEX

## A

Abas, 262.  
**ABRIOL, RUFINO**, Amoebic abscess of the liver among Filipinos, 121.  
 Abscess, amoebic, of the liver among Filipinos, 121.  
 Acclimatization, experimental, to the tropical sun, 1.  
 Age, incidence of, atheroma, and aneurisms as seen in autopsies of Filipinos, 233.  
 Agong, 270.  
 Akhir, 266.  
 Alathata, 270.  
 Alem, 273.  
 Ambystoma, 183.  
 Amoeba, 25, 123.  
 Amoebic abscess of the liver among Filipinos, 121.  
 Anaplasma centrale, 286.  
 Anaplasma marginale Theiler, a disease in cattle in the Philippine Islands similar to that caused by, 281.  
 Anatomicopathologic lesions in one thousand Filipino children under five years, 51.  
 Aneurisms, incidence of age, and atheroma, as seen in autopsies of Filipinos, 233  
 Anga, 262.  
 Ankylostoma, 66, 136.  
 Asnl, 265.  
 Ascaris, 25, 66, 158, 204.  
     lumbricoides, 66, 136.  
 Atheroma, incidence of age, and aneurisms as seen in autopsies of Filipinos, 233.  
 Aval, 266.  
 Autopsies, incidence of age, atheroma, and aneurisms as seen in, of Filipinos, 233.

## B

Babesia bigemina, 286.  
 Bacatau, 262.  
*Bacillus leprae*, the varying morphology of, and the routine microscopic examination of nasal mucus in lepers, 115.  
     subtilis, 182.  
 Bacteriologic investigation of faeces and bile of cholera cases and cholera carriers, 85.  
 Bagu, 275.  
 Bakil, 262.  
 Balantidial colitis, two cases of, 149.  
 Balantidium coli, 140.  
 Barahama, 268.  
 Bariceab, 275.  
 Barirang, 262.  
 Batuc, 262.

## B

Beneg, 262.  
 Beriberi, infantile, 71.  
 Bibesia mutans, 287.  
 Bilas, 262.  
 Bile, bacteriologic investigation of faeces and, of cholera cases and cholera carriers, 85.  
     the influence of, upon the distribution of cholera vibrios in the digestive system of experimental cholera carriers, 28.

## Bingki

Bisan, 268.  
 Blastocystis hominis, 158.  
 Blood cells, substitution of human, by monkey's red corpuscles in performing the complement fixation test for syphilis, 249.  
 Boophilus decoloratus, 287.

**BOYNTON, WILLIAM HUTCHINS**, A disease in cattle in the Philippine Islands similar to that caused by *Anaplasma marginale* Theiler, 281.

## Bronchopneumonia

Bubug, 275.  
 Buguis-casila, 262.  
 Buguis-murus, 262.  
 Bulaiacau, 271.  
 Bulay, 262.  
 Bundy, 276.  
 Bungalawan, 271.  
 Bungeaut, 262.  
 Bunug, 262.  
 Buransi, 262. \*
 Busudl, 263.  
 Buyo, 275.

## C

Cabig, 268.  
 Cabutá, 269.  
 Cagau, 265.  
 Caludusan, 263.  
 Calugú, 263.  
 Catal or ful, 263.  
 Cattle, a disease in, in the Philippine Islands similar to that caused by *Anaplasma marginale* Theiler, 281.  
 Catú, 263.  
 Caturay, 276.  
 Chemicals, a survey of certain, with regard to their bactericidal action on cholera vibrios within the body of experimental cholera carriers, 215.  
 Children, study of the anatomicopathologic lesions in one thousand Filipino, under five years, 51.  
 Chiuleaida, 269.  
 Chiuljigula, 269.

**Cholera, Asiatic**, 64.

**Cholera carriers**, a survey of certain chemicals with regard to their bactericidal action on cholera vibrios within the body of experimental, 215; bacteriologic investigation of feces and bile of cholera cases and, 85; experimental, and immunity, 43; the influence of bile upon the distribution of cholera vibrios in the digestive system of experimental, 23.

**Cholera patients**, essential factor in the treatment of pregnant, 191.

**Corpuscles**, substitution of human blood cells by monkey's red, in performing the complement fixation test for syphilis, 249.

**Cosmibotus platyrurus**, 182.

**Cotabato Province**, Mohammedan medical practice in, 261.

**CROWELL, B. C., and JOHNSTON, JOHN A.**, Bacteriologic investigation of feces and bile of cholera cases and cholera carriers, 85.

**Culintañgan**, 270.

**Curbau**, 263.

**Cutica**, 268.

#### D

**Dalima**, 271.

**Daranti**, 263.

**Degeneration of peripheral nerves**, 169.

**Dipylidium caninum**, 64.

**Disease in cattle in the Philippine Islands similar to that caused by Anaplasma marginale Theiler**, 281.

**Dudsul**, 263.

#### E

**Echinostoma echinatum**, 206.

**ilocanum**, 203.

**malayanum**, 206.

**Entamoeba histolytica**, 102.

#### F

**Feces**, bacteriologic investigation of bile and of cholera cases and cholera carriers, 85. **Fascioletta ilocana**, 206.

#### G

**Garruk**, 263.

**GARCIA, FAUSTINO**, Common intestinal parasites, 25.

**Garu**, 271.

**Gastrointestinal diseases**, 61.

**Gatasan**, 271.

**GIBSON, ROBERT B.**, *see RUTH, EDWARD S.*, 181.

**GOMEZ, LIPORIO**, Mohammedan medical practice in Cotabato Province, 261.

**GUAZON, POTENCIANO**, A case of advanced pregnancy in the broad ligament, 83.

**Guimadil-agir**, 269.

**Guimadil-aual**, 269.

**Gusan**, 275.

#### H

**Haguimat**, 277.

**Hemidactylus frenatus**, 182.

**lozonensis**, 182.

**HILARIO, J. S., and WHARTON, L. D.**, *Echinostoma ilocanum* (Garrison). A report of five cases and a contribution to the anatomy of the fluke, 203.

**Hookworms**, 26.

**Human blood cells**, substitution of, by monkey's red corpuscles in performing the complement fixation test for syphilis, 249.

**Hymenolepis nana**, 25.

#### I

**Ibis**, 273.

**Ibul**, *see Catal.*

**Ila**, 263.

**Immunity, experimental cholera carriers and**, 43.

**Ing**, 263.

**Intestinal parasites, common**, 25.

**Ipol**, 263.

#### J

**JOHNSTON, JOHN A.**, The varying morphology of *Bacillus leprae* and the routine microscopic examination of nasal mucus in lepers, 116. *See also CROWELL, B. C.*, 85.

#### K

**Kahn**, 268.

**Kaluli**, 263.

**Karumungan**, 276.

**Katayatay**, 273.

**Kihala**, 270.

**Kildin**, 277.

**Kisul**, 273.

**Kudep**, 263.

#### L

**Lacap**, 263.

**Lagundi**, 276.

**Lalasnbay**, 275.

**Lamlam**, 263.

**Lañgilaú**, 268.

**Lebag**, 263.

**Lepers**, the varying morphology of *Bacillus leprae* and the routine microscopic examination of nasal mucus in, 116.

**Lesions, study of the anatomicopathologic in one thousand Filipino children under five years**, 51.

**Ligament**, a case of advanced pregnancy in the broad, 83.

**Liver**, amoebic abscess of the, among Filipinos, 121.

**Lizard**, disappearance of the pigment in the melanophore of Philippine house, 181.

**LOWELL, PAUL McC.**, Essential factor in the treatment of pregnant cholera patients, 191.

**Lubigan**, 278.

**Lujur**, 268.

**Lumasá**, 268.

#### M

**Macabuhay**, 275.

**Magarib**, 268.

**Magudu**, 263.

**on rugu**, 263.

**Maguiakaní**, 271.

**Maisuara**, 268.

- Malaria, 81.  
 Malung, 274.  
**MANALANG, C.**, Degeneration of peripheral nerves, 169.  
 Mancueulam, 265.  
**Manila Medical Society**, Proceedings of the April 2 meeting, 255; of the August 6 meeting, 257; of the February 18 meeting, 105; of the January 6 meeting, 41; of the March 5 meeting, 165; of the October 1 meeting, 298.  
**MANLOVE, C. H.**, Incidence of age, atherosclerosis, and aneurisms as seen in autopsies of Filipinos, 233; Two cases of Balantidial colitis, 149.  
 Manu-manukan, 268.  
 Mapansi, 263.  
 Mapasalay, 278.  
 Muuaga, 263.  
 Mayau, 263.  
 Mayau-matingau, 263.  
 Medical practice, Mohammedan, in Cotabato Province, 261.  
 Melanophore, disappearance of the pigment in the, of Philippine house lizards, 181.  
**MENDOZA-GUASON, MARIA PAZ**, Study of the anatomicopathologic lesions in one thousand Filipino children under five years, 51.  
 Menigitis, 79.  
 Mohammedan medical practice in Cotabato Province, 261.  
 Monads, 26.  
 Monkey's red corpuscles, substitution of human blood cells by, in performing the complement fixation test for syphilis, 249.  
**MONSERRAT, CARLOS**, see SCHÖBL, OTTO, 249.  
 Morphology of *Bacillus leprae* and the routine microscopic examination of nasal mucus in lepers, 115.  
 Mujarram, 260.  
 Muta-mudu, 263.
- N**
- Nasadir, 263.  
 Nerves, degeneration of peripheral, 169.
- O**
- Oxyuris*, 26, 66.  
*vermicularis*, 132.
- P**
- Pagubad, 270.  
 Pagupat, 270.  
 Palgu as ragat, 270.  
 Pali, 263.  
 Pamagat, 263.  
 Pamari, 263.  
 Pambabuyen, 263.  
 Pamunus, 263.  
 Pamuti, 263.  
 Panaman, 265.  
 Panau, 268.  
 Pandidang, 270.  
**PANGANIBAN, G. S.**, see SCHÖBL, OTTO, 48.
- Panigater, 263.  
 Panú, 263.  
 Panunditung, 271.  
 Papapuntac, 266.  
 Parasite, common intestinal, 25.  
 Parasites, intestinal, 66.  
 Paemé, 263.  
 Patauall, 275.  
 Patija, 272.  
 Pnubatan, 276.  
 Pedcandui, 270.  
 Pedsa, 263.  
 Pedshay, 270.  
 Peripheral nerves, degeneration of, 169.  
*Peropus mutillatus*, 182.  
 Philippine Islands Medical Association, meeting held January 6, 42; minutes of the, 296.  
 Pigket or nasadir, 263.  
 Pigment, disappearance of the, in the melanophore of Philippine house lizards, 181.  
 Pithecius, 1.  
 Pneumonia, lobar, 78.  
 Pregnancy, a case of advanced, in the broad ligament, 33.  
 Pregnant cholera patients, treatment of, 191.  
 Putic, 263.
- R**
- Rabi-el-agir, 269.  
 Rabi-el-aul, 269.  
 Raguin, 269.  
 Ramellan, 269.  
 Rastun, 263.  
 Ratiun, 263.  
 Rayor, 264.  
*Rhipicephalus simus*, 287.  
**RUTH, EDWARD S.** and **GIBSON, ROBERT B.**, Disappearance of the pigment in the melanophore of Philippine house lizards, 181.
- S**
- Saandana, 271.  
 Saguimp, 264.  
*Sagulinga busau*, 273.  
 Saitan, 274.  
 Sakit, 264.  
     a mama, 264.  
 Salabi, 264.  
 Salamat-iblis, 264.  
 Selaysina, 273.  
 Sailau, 264.  
 Salimbanzan, 270.  
 Samaya, 265.  
 Sambung, 278.  
 Sanki, 273.  
 Sapa, 266.  
 Sapar, 269.  
**SCHÖBL, OTTO**, A survey of certain chemicals with regard to their bactericidal action on cholera vibrios within the body of experimental cholera carriers, 215; The influence of bile upon the distribution of cholera vibrios in the digestive system of experimental cholera carriers, 28.

- |  |   |
|--|---|
| <p>SCHÜBL, OTTO, and MONSERRAT, CARLOS. Substitution of human blood cells by monkey's red corpuscles in performing the complement fixation test for syphilis, 249.</p> <p>SCHÜBL, OTTO, and PANGANIBAN, G. S., Experimental cholera carriers and immunity, 48.</p> <p>Sedased, 264.</p> <p>SHAKLEE, ALFRED OGLE, Experimental acclimatization to the tropical sun, 1.</p> <p>Sibucso, 273.</p> <p>Sirungan, 263.</p> <p>Sry, 268.</p> <p>Strongyloides, 25.</p> <p>Subu, 268.</p> <p>Syphilis, substitution of human blood cells by monkey's red corpuscles in performing the complement fixation test for, 249.</p> | <p>Tingan, 276.</p> <p>Trichoocephalus dispar, 186.</p> <p>Trichuris, 25, 66, 151, 204.<br/>trichiura, 28.</p> <p>Tropical sun, experimental acclimatization to the, 1.</p> <p>Tuberculosis, 88.</p> <p>Tudi, 276.</p> <p>Tumiti sa nana, 264.</p> <p>Tumors, 81.</p> <p>Tunki, 278.</p> <p>Tutugan, 271.</p> <p>Typhoid fever, 80.</p> |
| T  | U   |
| <p>Tabib, 269.</p> <p>Tienia, 25.</p> <p>Taguitic, 264.</p> <p>Takendi, 264.</p> <p>Tanigan-tanigan, 275.</p> <p>Tangung, 268.</p> <p>Tauacal, 265.</p> <p>Tebpig, 264.</p> <p>Tigbao, 276.</p> <p>Tikuas, 275.</p> <p>Tindig, 266.</p> <p>Tinemban sa busau, 265.</p>   | <p>Uallan, 276.</p> <p>Usir, 264.</p> <p>Ugam, 264.</p> <p>Ulag, 264.</p> <p>Ulapiig, 264.</p> <p>Uled, 264.</p> <p>Umau, 264.</p> <p>Umes, 264.</p> <p>Umur, 265.</p> <p>Urae a ating, 264.</p>  |
|  | W   |
|  | <p>Wactu, 268.</p>  |
|  | X   |
|  | <p>Xaual, 269.</p>  |
|  | Z   |
|  | <p>Zaban, 269.</p>  |



WHARTON, L. D., see HILARIO, J. S., 203.





